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dl-GLUTAMIC ACID HYDROCHLORIDE IN TREATMENT OF PETIT MAL AND PSYCHOMOTOR SEIZURES

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In the majority of cases the treatment of epilepsy is moderately satisfactory.[1] Grand mal attacks are controlled completely or reduced in frequency by phenytoin or phenytoin-phenobarbital combinations in the majority of cases. Psychomotor attacks yield less readily to anticonvulsant therapy. Petit mal attacks are infrequently affected by medication but respond favorably to fasting [2] and the ketogenic diet.[3]

The hypothesis advanced by Wilder [3] and supported by Keith's experiments [4] that the mechanism of the ketogenic diet depended on the sedative effect of the ketone bodies was not generally accepted. Fay [5] and McQuarrie [6] attributed the effect to dehydration incidental to ketosis. Bridge and Iob [7] were doubtful that either to acidosis or to ketosis alone could be ascribed anticonvulsant properties.

Maintenance of a dietary regimen that will produce ketonuria is not a simple task. Hospitalization and an intensive educational program for the patient and his parents are necessary. A search for acidosis producing drugs was the outgrowth of these disadvantages of the ketogenic dietary regimen. We have used ammonium chloride (2 cases included in this series) without striking results. Azosulfamide [8] reduced the frequency of seizures moderately and concomitantly lowered the p_H of the blood. Brilliant vital red also seemed to have a moderate anticonvulsant effect.[9]

Putnam and Merritt [10] suggested that the "physiologic" anticonvulsants dextrose, carbon dioxide, pyruvic acid and acetoacetic acid and the synthetic anticonvulsants produce their effect by giving rise to an acid milieu within or about nerve cells. The synthetic anticonvulsants are of a composition which suggests that they are broken down by cellular activity, perhaps chiefly in the brain, to stable acid products such as benzoic acid. Anticonvulsant treatment of epilepsy is suggested as a substitution rather than drug therapy.

The use of *dl*-glutamic acid was suggested by one of us (H. W.) on the basis of the following considerations:

It is known that some racemic amino acids, among them *dl*-glutamic acid, give rise to the excretion of the unnatural isomer in the urine when administered to animals. If *d*-glutamic acid has a similar metabolic inertia [11] in human metabolism, 1 mole of *d*-glutamic acid hydrochloride should furnish 1 mole of hydrochloric acid and two carboxyl groups of which one would be available for acidification. The *l*-glutamic acid hydrochloride also furnishes one equivalent of hydrochloric acid.

Furthermore, *l*-glutamic acid has been stated to be intimately related to brain metabolism. It is the only amino acid known to be metabolized by slices of brain tissue.[12] Brain tissue contains an enzyme which synthesizes glutamine from *l*-glutamic acid and ammonia, decreasing by this mechanism the concentration of free ammonia in the tissue.[13]

Patients with seizures usually associated with slow wave activity in the electroencephalogram were selected for treatment. The amount of the amino acid hydrochloride required to maintain the p_H of the urine at about 5.0 was 4 Gm. three times a day. Larger doses,

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1. Merritt, H. H., and Putnam, Tracy J.: Further Experiences with the Use of Sodium Diphenyl Hydantoinate in the Treatment of Convulsive Disorders, Am. J. Psychiat. **96:** 1023-1027 (March) 1940.

2. Geyelin, H. R.: Fasting as a Method for Treating Epilepsy, M. Rec. **99:** 1037-1039, 1921.

3. Wilder, R. M.: The Effect of Ketonemia on the Course of Epilepsy, Mayo Clinic Bull. **2:** 307, 1921. Helmholz, H. F., and Keith, H. M.: Ten Years' Experience in the Treatment of Epilepsy with the Ketogenic Diet, Arch. Neurol. & Psychiat. **29:** 808-812 (April) 1933. Helmholz, H. F., and Goldstein, Moe: Results of Fifteen Years' Experience with the Ketogenic Diet in Treatment of Epilepsy in Children, Proc. Staff. Meet., Mayo Clin. **12:** 433-436 (July 14) 1937; Am. J. Psychiat. **94:** 1205-1214 (March) 1938. Keith, H. M.: The Treatment of Epilepsy in Children, Canad. M. A. J. **37:** 485-489 (Nov.) 1937. Barborka, C. J.: Epilepsy in Adults: Results of Treatment by Ketogenic Diet in One Hundred Cases of Epilepsy in Adults, Arch. Neurol. & Psychiat. **23:** 904-914 (May) 1930. Peterman, M. G.: Convulsions in Childhood; Review of 1,000 Cases, J. A. M. A. **113:** 194-198 (July 15) 1939. Talbot, F. B.: Treatment of Epilepsy, New York, Macmillan Company, 1930.

4. Keith, H. M.: The Effect of Various Factors on Experimentally Produced Convulsions, Am. J. Dis. Child. **41:** 532-543 (March) 1931; Further Studies on the Control of Experimentally Produced Convulsions, J. Pharmacol. & Exper. Therap. **44:** 449-455 (April) 1932; Factors Influencing Experimentally Produced Convulsions, Arch. Neurol. & Psychiat. **29:** 148-154 (Jan.) 1933.

5. Fay, Temple: The Therapeutic Effect of Dehydration on Epileptic Patients, Arch. Neurol. & Psychiat. **23:** 920-945 (May) 1930.

6. McQuarrie, Irvine: Epilepsy in Children: The Relationship of Water Balance to the Occurrence of Seizures, Am. J. Dis. Child. **38:** 451-467 (Sept.) 1929.

7. Bridge, E. M., and Iob, L. V.: The Mechanism of the Ketogenic Diet in Epilepsy, Bull. Johns Hopkins Hosp. **48:** 373-389 (June) 1931.

8. Cohen, M. E., and Cobb, Stanley: Anticonvulsive Action of Neoprontosil in Epileptic Patients, Tr. Am. Neurol. A. **66:** 199-202, 1940.

9. Osgood, Rudolf, and Robinson, L. J.: Brilliant Vital Red as an Anticonvulsant in Treatment of Epilepsy: A Study of 13 Cases, Arch. Neurol. & Psychiat. **40:** 1178-1204 (Dec.) 1938. Cobb, Stanley; Cohen, M. E., and Ney, Joseph: Anticonvulsant Action of Vital Dyes, ibid. **40:** 1156-1177 (Dec.) 1938.

10. Putnam, T. J., and Merritt, H. H.: Chemistry of Anticonvulsant Drugs, Arch. Neurol. & Psychiat. **45:** 505-516 (March) 1941.

11. Ratner, S.; Weissman, N., and Schoenheimer, R.: The Excretion of the Unnatural Isomers of Lysine and Glutamic Acid Investigated with the Aid of Isotopes, Meet. Am. Chem. Soc., Div. Biol. Chem., September 1941. Waelsch, H., and Rittenberg, D.: Glutathione: Metabolism of Glutathione Studied with Isotopic Ammonia and Glutamic Acid, J. Biol. Chem. **144:** 53-58 (June) 1942.

12. Weil-Malherbe, H.: Studies on Brain Metabolism: I. The Metabolism of Glutamic Acid in Brain, Biochem. J. **30:** 665 (April) 1936.

13. Krebs, H. A.: The Synthesis of Glutamine from Glutamic Acid and Ammonia, and the Enzymic Hydrolysis of Glutamine in Animal Tissues, Biochem. J. **29:** 1951 (Aug.) 1935.

16 and 20 Gm., were administered in 2 cases. Oral administration of the drug in dilute solution or capsules was seldom associated with gastric distress. Anticonvulsant therapy, though ineffective, was continued throughout the trial period.

Nitrazine paper tests of the morning specimen of urine were made by the patient in the majority of instances. This test gives the relative degree of acidity within half a p_H unit approximately. The *dl*-glutamic acid hydrochloride was prepared by one of us (H. W.).

REPORT OF CASES

CASE 1.—K. Mac., aged 12 years, had had petit mal seizures which recurred at a frequency of about forty to fifty a day for four years. A six months trial of the ketogenic diet reduced the seizures moderately. The patient refused to continue the rigid regimen.

General physical and neurologic examinations were within normal limits. Negative laboratory tests included a complete blood count, urinalysis, a blood Kline test, psychometric studies and x-ray examination of the skull. Frequent petit mal seizures were accompanied by typical three per second wave and spike formations in all leads of the electroencephalogram.

Maximum tolerated doses of phenytoin sodium and phenobarbital reduced the seizures slightly; that is, the number of days on which fifty seizures occurred were reduced. *dl*-Glutamic acid hydrochloride administration was accompanied by a sharp decrease in seizures. The dose required to maintain a urinary p_H of about 5.0 was 12 Gm. daily. Attacks were reduced to about five to twenty-five a day in contrast to twenty-five to fifty.

In addition to the reduction in seizures, the patient's parents and instructors in school noted a decided improvement in the patient's personality. He accepted disciplinary measures without prolonged arguments. He was more congenial, cooperative and affable. Peculiar egocentric aptitudes were decreased. Concentration and application in his school work were improved.

Ammonium chloride (4.0 Gm. daily) administered for five weeks failed to influence the frequency or severity of seizures.

In this case *dl*-glutamic acid hydrochloride reduced the total number of seizures and produced an improved physical and mental alertness pleasing to patient, parents and other interested parties. Ammonium chloride proved ineffective.

CASE 2.—M. B., aged 13 years, had had petit mal seizures (fifteen to thirty daily) for three to four months. Mild depressions were noted occasionally as a result of the recurrent seizures. General physical and neurologic examinations gave negative results. Negative laboratory examinations included a blood count, urinalysis, a blood Kline test, an x-ray examination of the skull, a pneumoencephalogram and psychometric studies. The electroencephalogram showed a pattern commonly associated with convulsive disorders, petit mal type.

Phenytoin sodium and phenobarbital therapy was ineffective. *dl*-Glutamic acid hydrochloride reduced the number of seizures to two to five a day. The p_H of the urine was lowered to 5.0 in forty-eight hours and maintained at this level. The decrease in frequency of the seizures paralleled the lower p_H values of the urine.

The ingestion of the drug was accompanied by an immediate improvement in the clinical condition of the patient. In the past nine months the drug has repeatedly been discontinued with the result that the symptoms have immediately recurred. Improvement has followed readministration of the drug in adequate doses.

The decrease in seizures was accompanied by an improved mental and physical alertness. Exacerbation and remissions of symptoms were closely correlated with glutamic acid therapy.

CASE 3.—C. H., aged 7 years, had recurrent petit mal seizures which had resisted phenytoin sodium, phenobarbital and a combination phenytoin-phenobarbital therapy. General physical and neurologic examinations gave negative results. Negative laboratory examinations included x-ray examinations of the skull, psychometric studies, urinalysis, a blood count and a blood Kline test. The electroencephalogram revealed a pattern commonly associated with convulsive disorder, petit mal type.

Following the determination of tolerant doses of phenytoin sodium and phenobarbital, *dl*-glutamic acid hydrochloride was administered. The drug in concentrated solution caused severe gastric distress. He later rejected dilute solution (in water, milk, fruit juices). During this period of inadequate treatment petit mal seizures increased from six to ten to twenty to twenty-five a day.

This is the lone instance of severe gastric distress caused by the drug. Obviously the concentrated solution caused the gastric discomfort. The increased frequency of seizures was related to the emotional response rather than to the effect of the drug. Petit mal seizures are often increased in frequency and severity by excitement, worry, stress and strain.

CASE 4.—S. K., a girl aged 8 years, had a recurrent abdominal pain which was first noted at the age of 6 years. Acute pain followed by vomiting recurred weekly for four months. The recurrence of pain ceased, but frequent short periods of staring were noted by the parents. Subsequently this symptom was accompanied by right sided signs (facial asymmetry, clonic movements of the right hand and face and a tendency to fall to the right). Though predominantly on the right, seizures have been noted to occur on the left side for periods of as long as two weeks. The frequency of seizures varied from one hundred to two hundred a day. Personality disturbances (disobedience, destructiveness, cruelty to her playmates and indifference) were not related to the frequency of seizures or medication and responded readily to the use of customary disciplinary measures.

Pneumoencephalograms have been normal on three occasions. Psychometric studies disclose an average intelligence (intelligence quotient 101 Stanford-Binet, 114 Arthur). The electroencephalogram repeatedly demonstrated a focus of slow wave activity in the left temporoparietal area.

Right facial weakness and impairment of motor function, voluntary and involuntary, in the right arm and leg has progressed slowly. She is now unable to write with her right hand.

Various combinations of phenytoin sodium, phenobarbital, thyroid, *dl*-pyrrolidone carboxylic acid and *dl*-glutamic acid hydrochlorideo, ammonium chloride, ketogenic diet, nicotinic acid and methyl ethyl phenobarbital were administered. Phenobarbital in increasing dosage to 0.3 Gm. daily was moderately effective over the longest period of time any one drug was administered. *dl*-Glutamic acid hydrochloride in combination with phenobarbital was strikingly effective. Except for an increase in the number of seizures accompanying the excitement of going home, the greatest number of days on which twenty-five seizures or less could be counted was noted within the ensuing two months. Five seizures or less were noted for two consecutive weeks. Seizures recurred at the pretreatment frequency immediately after withdrawal of the drug. Renewal of treatment was not accompanied by a decrease in frequency of the attacks, but this fact is difficult to evaluate because thyroid in toxic doses was administered during the second trial period.

Methyl ethyl phenobarbital in conjunction with nicotinic acid and phenytoin sodium was also accompanied by a striking improvement. Initially the seizures decreased in severity and later in frequency. For two months from one to ten seizures occurred daily, accompanied by a moderate return of function of the right hand. Unavoidably methyl ethyl phenobarbital was discontinued, and the seizures immediately recurred.

On readmission to the hospital, right sided seizures recurred at intervals of five to fifteen minutes.

Evaluation of medication is difficult, but we were impressed with the response accompanying *dl*-glutamic acid hydrochloride therapy, in conjunction with phenobarbital.

CASE 5.—J. R., a youth aged 21, had recurrent psychomotor seizures preceded for an hour of repeated myoclonic twitches and mental confusion, which were decreased by phenytoin sodium, phenobarbital and thyroid.

General physical and neurologic examinations were negative. Negative laboratory examinations included a complete blood count, urinalysis, x-ray examinations of the skull, pneumoencephalogram, psychometric studies and blood Kline and sugar tolerance tests. The basal metabolic rate was minus 18, minus 22 and minus 20 and serum cholesterol was 271 mg. per hundred cubic centimeters. The electroencephalogram showed a pattern commonly associated with convulsive disorders.

Seizures recurred at weekly intervals without treatment. Administration of phenytoin sodium, phenobarbital and thyroid in maximum tolerated doses was accompanied by a reduction in seizures, namely one attack every one to three weeks. Extra phenytoin sodium and phenobarbital administered after the onset of the aura had no effect on the impending seizures.

Ammonium chloride (4 to 6 Gm. daily) reduced the frequency of seizures slightly, but the appearance of severe acne prevented its prolonged administration.

After addition of *dl*-glutamic acid hydrochloride to the foregoing combination, seizures could be prevented by the use of phenytoin sodium (0.1 Gm.) and phenobarbital (0.1 Gm.) during the phase of the aura. Attacks were prevented for a period of three months, the longest interseizure interval in two years.

The dosage required to maintain a urinary p_H of 4.5 to 5.0 was 12 to 20 Gm.

Equally encouraging was the subjective improvement. Parents, friends and business associates volunteered the information that the patient's behavior had changed for the better. He was decidedly more affable. His gymnasium instructor reported an improved physical alertness. His assistant noted an increased mental acuity. For the first time he desired and sought social contacts outside the family circle. Hospital attendants noted a decided improvement in cooperation in respect to both hospital routine and clinical tests.

In this case decided psychologic improvement followed an increased mental and physical alertness, which has aided measurably in social and economic rehabilitation. Seizures recurred at one to four week intervals following withdrawal of the drug irrespective of supplementary medication after the onset of the aura. Though the major portion of the psychologic improvement has been maintained, there has been no progress on other forms of medication.

A regimen designed to determine the effect of *dl*-glutamic acid hydrochloride on the acid-base balance of the blood has recently been instituted. Twelve Gm. doses of the drug have failed to alter the acid-base balance and likewise to affect the frequency of seizures. Failure to respond is probably associated with an intake of excessive doses of thyroid, as in case 4. Symptoms of thyroid intoxication (weakness, sweating, fatigue, restlessness and emotional lability) have been noted recently. After thyroid was discontinued the favorable response to glutamic acid has been reproduced.

Even though seizures may be aborted by supplementary therapy after the onset of the aura, the latter occurs more frequently during the period of *dl*-glutamic acid hydrochloride therapy. The aura is associated with the fast activity and the psychomotor seizures with slow wave activity in the electroencephalogram. This suggests that the drug is effective only in seizures associated with slow wave activity. Improved mental and physical alertness have aided measurably in social and economic rehabilitation.

CASE 6.—B. J., a man aged 25, had a moderately severe head injury at the age of 3 years; this was the only suggestion of an etiologic factor disclosed in the history. Unlike his brother and sister, the patient had always been irritable, restless, emotionally labile (temper tantrums, indifference, depressions) and retarded mentally (school work difficult and far below standards of the family). Anxiety states resulting from recurrent periods of mental dulness prevented employment. He resented his mother's habit of repeatedly recounting his inadequacies to him and others. Though he honestly attempted to maintain employment, recurrent grand mal, petit mal, psychic equivalents and periods of mental dulness prevented contact with the public.

Hemiatrophy of the left arm and leg suggested the presence of diffuse involvement of the right hemisphere of the brain, probably post-traumatic in origin. Confirmation of this opinion was demonstrated in the electroencephalogram, namely a diffuse abnormal pattern was most severe in the right frontal area.

Except for psychic equivalents and periods of mental dulness the patient has been symptom free with phenytoin sodium (0.4 Gm.) and phenobarbital (0.1 Gm.) therapy.

dl-Glutamic acid hydrochloride was administered in 12 Gm. doses daily. Objectively the psychic equivalents and periods of mental dulness were unaffected. Subjectively interseizure periods were accompanied by an increased mental and physical alertness new to the patient. Though not dramatic, the effect was definitely encouraging to him. The drug was discontinued suddenly six weeks later, following which symptoms were intensified and a grand mal seizure occurred, the first in seven months. Readministration of the drug was accompanied by an improvement similar to the previous one. Exacerbation of the symptoms again followed interruption of treatment four weeks later.

In this case subjective improvement accompanied ingestion of *dl*-glutamic acid hydrochloride. Interruption of treatment was followed by an exacerbation of symptoms, and improvement occurred on reinstitution of therapy. Exacerbation of symptoms commonly associated with irregular inadequate treatment of epilepsy is exemplified in this case.

CASE 7.—M. B. S., a woman aged 41, had onset of seizures at the age of 20. Severe social, educational and economic restrictions have been a serious handicap. Seizures were strikingly reduced by phenytoin sodium. Personality disturbances combined with social maladjustment prevented a satisfactory rehabilitation following control of the seizures. Severe emotional instability is far more incapacitating than infrequent psychic equivalents, grand mal, petit mal and psychomotor attacks.

General physical and neurologic examinations have been repeatedly negative. Negative laboratory studies include x-ray examinations of the skull, psychometrics, urinalysis, complete blood count and blood sugar determination. The electroencephalogram disclosed a pattern consistent with convulsive disorder.

dl-Glutamic acid hydrochloride in conjunction with phenytoin therapy reduced petit mal seizures and psychic equivalents. A daily dose of 12 Gm. maintained a urinary p_H of about 5.0. Psychomotor and grand mal attacks were also reduced in frequency.

Improved mental and physical alertness was noted objectively and subjectively. Tolerance of the opinions of others was noticeably improved. Insight was acquired into her pronounced introversion, egocentric responses to minor stimuli, recurrent anxiety states and mild depressions. The efficiency with which she performed the details of her position as a librarian was augmented by the increased mental alertness. Gymnasium exercises became less laborious.

In this case petit mal attacks and psychic equivalents were decreased during the administration of *dl*-glutamic acid hydrochloride. A decided regression of mental and physical alertness followed withdrawal of the drug. Periodic rest in bed and a winter vacation were required to overcome a serious emotional instability.

CASE 8.—J. K., aged 20, had had recurrent grand mal seizures for three years. General physical and neurologic examinations were negative. Negative laboratory examinations included a complete blood count, blood Kline test, urinalysis, x-ray examinations of the skull and psychometric studies. The electroencephalogram demonstrated a pattern commonly associated with convulsive disorders.

dl-Glutamic acid hydrochloride in 12 Gm. daily doses reduced the urinary p_H to about 5.0. Increased mental and physical alertness was noted, but only to a slight degree.

Seizures occurred at the pretreatment rate of one every one to two weeks. Phenytoin sodium in 0.4 Gm. daily doses relieved the patient of seizures but had no effect on mental or physical alertness.

In this case, as noted previously, grand mal seizures were not affected by *dl*-glutamic acid hydrochloride.

COMMENT

Tolerance to *dl*-glutamic acid hydrochloride has proved surprisingly high. Gastrointestinal symptoms have been minimal. Objections to the taste have been alleviated by administration of the drug in capsules. Furunculosis has not occurred. Renal irritation has not been noted.

Improvement was noted in those cases in which the seizures are related to slow wave activity in the electroencephalogram, namely petit mal and psychomotor types. Seizures are decreased in frequency on medication which previously had been proved either ineffective or partially satisfactory. Petit mal seizures have been decreased from thirty to fifty to five to twenty-five daily in 1 case and from fifteen to twenty to three to five in another.

Universally, mental and physical alertness have been increased. The degree of improvement in mental efficiency cannot be correlated with the incidence of seizures. Without solicitation the patient, family and other interested parties have volunteered a favorable response to *dl*-glutamic acid therapy. Usually the patient is noted to be more energetic and happier, mood swings are less pronounced, behavior mannerisms are ameliorated and he is more congenial with associates.

Readministration of *dl*-glutamic acid hydrochloride was ineffective in 2 cases in both of which there was evidence of thyroid intoxication. Withdrawal of thyroid therapy was followed by a response similar to that of the initial treatment. In 2 other cases responses to readministration of the drug were quite similar to that of the initial treatment.

Ammonium chloride was administered in 2 cases (1 and 5). It proved ineffective in case 1, and severe acne resulted from its use in case 5.

Grand mal seizures were unaffected by the drug in 1 case (case 8). Focal motor cortical seizures and myoclonus likewise responded less favorably, as noted in cases 4 and 5 respectively.

It seems hardly necessary to emphasize that the beneficial effects of an additional aid in the treatment of epilepsy can be appraised only after a period of years. The preliminary results reported in this note may serve as a lead in further investigations. A comparison of the effect of *l*-glutamic and *d*-glutamic acid and their hydrochlorides as well as pyrrolidone carboxylic acid will show whether glutamic acid exerts a specific effect on the brain metabolism of epileptic patients.

SUMMARY

dl-Glutamic acid hydrochloride has been used in cases in conjunction with known anticonvulsant therapy. Seizures associated with slow wave activity in the electroencephalogram, namely petit mal and psychomotor types, were decreased in frequency. Increased mental and physical alertness have been most gratifying to patient, family and physician. Grand mal seizures were unaffected by the drug.

706 West 168th Street.

BULLIS FEVER

(LONE STAR FEVER—TICK FEVER)

AN ENDEMIC DISEASE OBSERVED AT BROOKE GENERAL HOSPITAL, FORT SAM HOUSTON, TEXAS

COLONEL JOHN C. WOODLAND
MAJOR MORDECAI M. McDOWELL
AND
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During the spring and summer of 1942 many patients suffering from various acute febrile diseases were admitted to the contagious disease section of Brooke General Hospital, Fort Sam Houston, Texas. Most of these illnesses presented no great diagnostic problem, being recognized as seasonal diseases, such as infections of the upper respiratory tract, tonsillitis and mild influenza. In April it became apparent that in this group of patients we were confronted with a number of acutely ill ones who were suffering from a clinical disease entity which had defied definite identification. A search of the available literature failed to throw any light on this perplexing problem, and no report of similar cases could be found.

There were several outstanding clinical features characteristic of this disease, i. e. an unusually low white blood cell count with moderate neutropenia, a severe postorbital and occipital headache, and a constant lymphadenitis varying from involvement of a few glands to general lymphadenopathy. All the soldiers comprising this group were members of the field force of Fort Sam Houston, Texas, and all gave a history of having been on maneuvers at Camp Bullis, Texas, an area used for the training of troops of this post a week or more prior to the onset of symptoms. In all cases there was evidence of multiple tick bites, especially of the legs and thighs. In a great many instances, ticks were found still clinging to the skin of the patient at the time of admission to the hospital. In each instance the tick was identified as Amblyomma americanum, commonly known as the Lone Star tick, so named because of the star shaped marking on its back. While chigger bites were a common experience to all commands, massive exposure to tick bites was peculiar to men who had been on duty in the maneuver area at Camp Bullis, Texas.

Soon recognizing the fact that we were dealing with a disease entity which defied identification, the commanding officer of the hospital, Col. George C. Beach, M. C., in a communication to the Office of the Surgeon General, U. S. Army, in July 1942, requested the services of consultants especially qualified in this field of medicine. In response to this request Drs. Kenneth F. Maxcy, Norman H. Topping and John C. Snyder of the Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army arrived at the hospital on July 8, 1942. After a thorough examination of the patients suffering from this disease still remaining in the hospital and after minute scrutiny of the clinical records of those who had been returned to duty, these consultants agreed that we were dealing with a definite disease found only in those soldiers who had been subjected to tick bites at Camp Bullis. They

Dr. Kenneth F. Maxcy, consultant to the Secretary of War, the Board for the Investigation and Control of Epidemic Diseases in the Army, Dr. Norman H. Topping, passed assistant surgeon of the United States Public Health Service, and Dr. John C. Snyder, staff member, Rockefeller Foundation, International Health Division, gave assistance, cooperation and constructive suggestions.

gave this syndrome a tentative designation of "tick bite fever." [1] It was their opinion that the epidemiologic evidence associating this illness with tick bites was highly suggestive but that the causative agent had not been conclusively identified, nor could it be definitely shown at that time that the disease was transmitted to man through the medium of the tick bite.

SYMPTOMS

Usually the onset was abrupt, with an initial chill or a chilly sensation ushering in the attack. Fever soon followed, the temperature ranging from 102 to 105 F. A few of the patients gave a history of prodromal symptoms for a few days prior to the onset of chill and fever. A great majority of the men complained of postorbital and occipital headache. Pronounced lassitude, prostration, anorexia and general weakness were noted during the febrile stage of the disease, and a few patients were nauseated and vomited. The fever lasted from four to fourteen days, with the temperature ranging from 102 to 105 F., and subsiding by lysis. In the average case the temperature was elevated for a little over five days. Convalescence was protracted, especially if the illness had been severe. Loss of weight was observed in a great many of the men, one patient losing more than 20 pounds (9 Kg.) within two weeks.

PHYSICAL FINDINGS

There was a paucity of physical findings in these patients, but all had an enlargement of at least one set of lymph glands and commonly general lymphadenopathy. The glands were easily palpable and in many instances were acutely tender. This glandular involvement persisted throughout the acute stage of the illness but disappeared rather promptly with the clearing of symptoms. The throat was usually slightly red and injected, but in none of the cases did the appearance resemble that usually seen in acute infection of the upper respiratory tract. In fact, complaints of involvement of the respiratory tract were conspicuous by their absence. Physical findings in the chest were normal, and roentgenograms failed to reveal any pathologic condition. In the more severe forms of the disease a maculopapular rash involving the trunk was noted. In some the eruption had the appearance of that seen in endemic typhus fever, and in others it resembled the rash seen in German measles. This manifestation of the syndrome rapidly faded and usually disappeared completely within forty-eight hours. In all instances examination revealed multiple tick bites.

LABORATORY FINDINGS

A constant laboratory finding characteristic of this disease was definite leukopenia occurring on or about the second or third day. In many instances the leukocyte count dropped to 3,000 and in one case to a low level of 1,750. With this abrupt drop in the total white blood cell count there was associated neutropenia, one patient having a polymorphonuclear count of 23 per cent. During the period of convalescence the total white blood cell count gradually approached normal; however, moderate lymphocytosis persisted up to the time of discharge. The red blood cell count and the hemoglobin determination remained normal throughout the course of the disease. Urinalyses yielded negative results except in a few instances in which an occasional trace of albumin was noted. Specimens of blood from 6 patients (cases 2, 3, 4, 30, 32 and 33 in the table) were examined at the National Institute of Health Laboratories for Q fever, Rocky Mountain spotted fever and typhus by the complement fixation method. Completely negative results were obtained. Blood specimens were examined by the Weil-Felix test using Proteus X_{19}, X_2 and X_k, with negative results. Agglutination determinations were accomplished for undulant fever, tularemia, typhoid and paratyphoid A and B with negative results. Repeated blood cultures and smears were found negative. The heterophile antibody reaction was negative in all cases examined. Laboratory investigation of the spinal fluid in several cases yielded normal findings. Biopsy of enlarged lymph glands disclosed only lymphoid hyperplasia.

CLINICAL COURSE

There were no deaths in this series of cases, the disease being self limited. The syndrome varied from a mild febrile illness of short duration to a severe debilitating prolonged disease with a protracted convalescence. In the more severe forms a rash resembling German measles, and at times typhus made its appearance early in the disease but disappeared within forty-eight hours. In about 10 per cent of the cases skin manifestations developed. The elevation in temperature continued for about five days in a majority of the cases and returned to normal by lysis. The temperature once it reached normal remained normal except in a few instances in which an occasional rise to 99 F. was noted. From clinical observation it is apparent that the incubation period of this disease is from seven to ten days.

TREATMENT

Patients were placed in bed during the acute stage of the illness and received routine nursing care. Codeine sulfate ½ to 1 grain (0.032 to 0.06 Gm.) with acetylsalicylic acid 5 to 10 grains (0.32 to 0.65 Gm.) every two or three hours and an ice bag to the head were used for relief of the severe headache. The intake of fluids was encouraged. Dextrose and saline solution was given intravenously to patients showing dehydration from deficiency of fluid intake or from vomiting. Hydrotherapy was employed as indicated to combat the febrile reaction and to make the patient more comfortable. Chemotherapy was used in a few of the cases but was observed only to increase the toxicity associated with this disease. The syndrome was self limited and apparently it conferred immunity, since no recurrences have been observed. In this series of cases no complications or sequelae have been noted.

A TYPICAL CASE

Sergeant W. A. S. (case 1 in the table), infantryman, Fort Sam Houston, Texas, with two years' military service, was admitted to the Brooke General Hospital on June 25, 1942 complaining of severe generalized headache of four or five hours' duration. His face was flushed as with fever, and he appeared acutely ill. The onset of illness was sudden with nausea, vomiting and severe headache. He had noted no prodromal symptoms and no symptoms involving the respiratory tract. He gave no history of previous serious illness. Occupation, habits and family history were noncontributory. He had been at Camp Bullis, Texas, for one week, June 13 to June 20 inclusive, and had returned to Fort Sam Houston five days prior to the onset of symptoms. While at Camp Bullis he suffered numerous tick and "chigger" bites. Physical examination revealed flushed skin and evidence of numerous insect bites on the abdomen and the legs. Moderate lymphadenopathy was found. Otherwise, physical examination gave negative results.

1. A Report of the Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Aug. 10, 1942.

Laboratory Findings.—Studies of the blood gave results as follows: June 26 the white blood cell count was 4,600 with 84 per cent polymorphonuclears, 13 per cent lymphocytes and 3 per cent monocytes; the blood smear was negative for malarial plasmodia. July 3 the white blood cell count was 3,550 with 41 per cent polymorphonuclears, 55 per cent lymphocytes and 4 per cent monocytes; the blood smear was negative for malarial plasmodia. July 11 the white blood cell count was 6,800 with 43 per cent polymorphonuclears, 52 per cent lymphocytes and 5 per cent monocytes. The red cell count and the hemoglobin content remained normal throughout.

1:80. The heterophile antibody reaction was negative. All the agglutinations were considered of no diagnostic significance.

Progress in Hospital.—June 27 the patient's temperature was still elevated. There were no complaints other than headache—no nausea, no vomiting and no rash. He was mentally clear. Neurologic examination gave entirely negative results. Some general weakness, lassitude and malaise were noted. June 30 the patient still had generalized enlargement of lymph glands, and his temperature was still elevated. He had no chills. July 4, the fourth afebrile day, he was ambulatory and completely asymptomatic. There was still generalized glandular

Composite Table of Bullis Fever Observed at Brooke General Hospital, Fort Sam Houston, Texas

Case	Duration of Fever, Days	White Blood Cell Count	Polymorphonuclears, per Cent	Lymphadenopathy	Exposure to Tick Bites	Comment
1	6	4,600 2,350 3,550 6,800	84 52 41 43	Yes	Yes	Severe headache, fever, nausea and vomiting
2	6	2,900 2,800 7,500	52 55 65	Yes	Yes	Fever only complaint
3	6	5,650 4,100 5,350 8,750	62 52 50 55	Yes	Yes	Severe postorbital and occipital headache, chill and fever
4	2	6,300 4,900 4,450 9,250	79 57 39 50	Yes	Yes	General malaise and headache
5	4	8,200 3,200 9,600	73 52 39	Yes	Yes	General malaise and headache
6	5	3,100 2,700 2,300 8,600	64 58 51 55	Yes	Yes	Backache, severe headache and fever
7	5	4,300 4,500 5,500 8,300	57 58 40 56	Yes	Yes	Aching in joints, headache and vomiting
8	7	3,750 3,100 5,250	80 67 55	Yes	Yes	Severe occipital headache and fever
9	4	11,500 4,750 6,950	80 53 54	Yes	Yes	Ill defined abdominal pain, headache and fever
10	9	3,700 7,850	40 52	Yes	Yes	Severe photophobia, occipital headache and fever
11	5	6,100 4,200 8,550	69 53 27	Yes	Yes	Chills, headache, fever and weakness
12	11	8,100 5,800 6,400	68 76 55	Yes	Yes	Generalized headache and fever
13	6	2,700 2,800 7,250 8,440	58 50 25 53	Yes	Yes	Temp. 104 F. for 3 days; gradual return to normal
14	5	6,500 2,100 7,900	81 50 50	Yes	Yes	Temp. 103 F. for 4 days; general malaise
15	5	2,400 1,750 7,500	85 63 55	Yes	Yes	Slight headache only complaint
16	6	3,700 6,300 7,300 6,450	40 63 24 52	Yes	Yes	Fever, backache, light chills, insidious onset
17	8	5,700 4,350 13,300	61 57 26	Yes	Yes	Fever, headache
18	6	12,000 4,000 5,250 8,900	24 62 47 45	Yes	Yes	Fever 6 days, highest temp. 104.4 F.; skin covered with tick bites
19	6	4,800 7,200 7,050 11,000	75 59 37 57	Yes	Yes	Fever only complaint
20	5	3,100 6,550	56 47	Yes	Yes	Severe myalgia
21	6	4,050 5,350 11,750	68 62 30	Yes	Yes	Chill, fever and aching
22	8	3,650 5,650	23 52	Yes	Yes	Chill, fever and general weakness
23	5	5,600 3,500 7,800	48 68 55	Yes	Yes	General aching
24	4	2,950 3,100 8,200	60 59 56	Yes	Yes	General malaise, nausea and vomiting
25	7	5,400 4,000 8,900	66 62 45	Yes	Yes	General malaise, backache and abdominal pain, not localized
26	5	4,200 8,700	72 60	Yes	Yes	Mild illness; headache, pain back of eyes
27	6	2,650 5,000 3,800 10,300	76 70 74 28	Yes	Yes	Frontal headache, anorexia, mild nausea and vomiting
28	4	3,250 4,550 6,800	61 66 32	Yes	Yes	No complaints except fever
29	3	3,500 3,200 5,000 8,600	62 39 28 52	Yes	Yes	Mild illness with slight occipital headache
30	5	3,900 3,200 5,000 8,600	77 39 28 52	Yes	Yes	Severe headache and slight chill at onset
31	5	4,000 5,500	59 64	Yes	Yes	No complaints except slight nausea
32	13	4,500 3,000 2,300 9,600	59 77 80 21	Yes	Yes	General malaise, headache
33	9	4,300 3,950 2,850 9,300	73 51 51 55	Yes	Yes	Generalized mottling of entire body—severe infectious disease

Complement fixation yielded negative results for Q fever, Rocky Mountain spotted fever, and typhus. Agglutination tests were negative, including Widal, Proteus X_{19}, X_2 and X_K, paratyphoid A and B, undulant fever and heterophile antibody reaction.

Urinalyses revealed only a slight trace of albumin during the febrile course of the disease.

The spinal fluid cell count was normal. The smear and the culture were negative. The protein and globulin contents were normal; the gold curve was flat; the chloride and sugar levels were normal. The spinal fluid pressure was normal. The Wassermann reaction was negative.

Tests for agglutination of Proteus X_{19}, X_2 and X_K were made on July 11, 14 and 17, with results as follows: July 11, Proteus X_{19} positive 1:160, X_2 negative, X_K negative; July 14, Proteus X_{19} positive 1:80, X_2 negative, X_K negative; July 17, Proteus X_{19} positive 1:80, X_2 positive 1:40, X_K positive

enlargement, which was the only constant physical derangement in this case. July 8 the lymphadenopathy was no longer discernible. There were no complaints. July 17 convalescence was considered as uneventful. The total white blood cell count was normal. The patient still showed moderate lymphocytosis.

A LABORATORY INVESTIGATION

The laboratory and field work to be reported now was accomplished by Col. H. R. Livesay, Medical Corps, and Capt. Morris Pollard, Veterinary Corps, of the Eighth Service Command Laboratory, Fort Sam Hous-

ton, Texas, in an attempt to determine the cause and the mode of transmission of this disease and to identify the vector.

Citrated and clotted bloods were inoculated intraperitoneally into rabbits and male guinea pigs. Spinal fluids with significant cytologic alteration were inoculated intracerebrally into guinea pigs, mice and rabbits. Spinal fluids and citrated bloods were also inoculated into developing 8 to 11 day old chick embryos by the chorioallantoic, yolk sac and intravenous routes. In addition, periodic serologic examinations were made for typhus, equine encephalomyelitis and lymphocytic choriomeningitis by the complement fixation test and for the Weil-Felix reaction.

All serologic examinations yielded negative results. The spinal fluids in several cases induced a mild transient febrile reaction in guinea pigs by intracerebral inoculation on the ninth day after inoculation. One serial passage at this point of brain material to normal guinea pigs reproduced this reaction with no apparent increase in virulence of the agent. No histologic abnormality could be detected in the brain tissue. When the febrile reaction developed in guinea pigs, brain material was transferred to chick embryos: five generations of chick embryos in series were killed after inoculation by the intravenous route within periods of six to nine days. There was no apparent increase in virulence of the agent by passage, and no lesions could be detected in the dead chick embryos. The spinal fluids induced no visible effect in mice or rats.

Temperature, pulse and respiration.

A consistent low grade febrile reaction was induced in guinea pigs with intraperitoneally inoculated citrated and clotted blood. This reaction developed on the ninth or tenth day after inoculation and usually lasted one or two days. No orchitis was observed in any of the guinea pigs inoculated; however, fibrinous peritonitis developed in 2 instances, and this material is now being transferred to normal guinea pigs.

One hundred and fifty ticks collected at random from Camp Bullis were pooled, triturated in saline solution and inoculated into male guinea pigs. One guinea pig inoculated intracerebrally with tick emulsion showed a one day temperature of 106.2 F., on the ninth day after inoculation.

Several deer, armadillos and jack rabbits were examined from Camp Bullis, and no lesions were detected grossly or histologically. Of the ticks collected the predominating type was Amblyomma americanum, and several belonging to Haemaphysalis leporis-palustris were removed from the jack rabbits.

No implication is being made as to the identity of the etiologic agent in these cases. The laboratory work is still in progress, and perhaps the results will merit a future report.

COMMENT AND CONCLUSION

The cases of "Bullis fever" comprising this group resemble in some respects the cases of Colorado tick fever reported by Topping, Cullyford and Davis.[2] In those cases, however, a typical saddle back type of fever curve was noted, the initial fever lasting two or three days, then becoming normal only to rise again. In the cases under our observation this type of temperature curve was not seen, except that in a few cases a secondary rise to 99 F. or slightly above was noted after a remission of one to three days. Lymphadenopathy, which was a constant finding in our series of cases, was not reported as found in the cases of Colorado tick fever. Dengue fever was thought of as a possible diagnosis, but the absence of exposure to mosquitoes and the clinical course of the disease aided in ruling out this condition as a possibility. Malaria was considered in view of the leukopenia, chills and fever, but this too was ruled out by the clinical course of the disease and by the negative blood smears. Acute mononucleosis was excluded by the negative heterophile antibody reaction, the absence of sore throat and the failure to find the typical white blood cells characteristic of this disease. Typhus and Rocky Mountain spotted fever were discarded as possibilities in view of the clinical course of the disease and the absence of laboratory findings in blood specimens. It is our opinion that Bullis fever constitutes a new disease entity heretofore undescribed.

All the men whose cases are included in this report gave a history of repeated and prolonged exposure to tick bites while undergoing training in the maneuver area known as Camp Bullis. This military reservation, approximately 20 miles west of Fort Sam Houston, Texas, has a heavy tick infestation.

Although no positive proof of the association of bites of Amblyomma americanum with this disease has been established, it is our opinion that further laboratory investigation will prove that this disease is transmitted to man through the tick bite. Recovery of the rickettsias of Rocky Mountain spotted fever from nymphs of A. americanum has been reported by R. R. Parker, G. M. Kohls and E. A. Steinhaus of the Rocky Mountain Laboratory of the National Institute of Health.[3] With this proof at hand it is reasonable to suspect that the disease under discussion is transmitted to man by the same vector.

In view of the fact that there will be heavy troop concentrations in rural areas during the present national emergency, and since it is felt that this disease is more widely distributed than has been recognized, we feel that the attention of medical officers should be called to the occurrence of this syndrome. Unless the possibility of the presence of this disease is kept constantly in mind, it will challenge one's diagnostic acumen, since it resembles in many respects other acute febrile illnesses.

It is apparent that this disease is increasing in frequency and severity in the San Antonio area. During the past two months [May and June 1943] 485 patients with the syndrome have been admitted to this hospital. A higher percentage of patients in this group have manifested the more serious symptoms, and there has been

2. Topping, N. H.; Cullyford, J. S., and Davis, G. E.: Colorado Tick Fever, Pub. Health Rep. **55**: 2224 (Nov. 29) 1940.

3. Amblyomma Americanum a Vector of Rocky Mountain Spotted Fever, Pub. Health Rep. **58**: 491 (March 19) 1943.

one fatality (May 21, 1943) attributed to this syndrome. In the patient who died the terminal clinical picture was that of severe agranulocytic angina and septicemia. A complete report on the autopsy material thus far has not been received. Grossly nothing was found that would aid in identifying this disease from a pathologic standpoint.)

ADJUVANT ALKALI THERAPY IN THE PREVENTION OF RENAL COMPLICATIONS FROM SULFADIAZINE

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Although the incidence of toxic reactions in general is lower with sulfadiazine therapy than with the other commonly employed sulfonamide drugs,[1] renal complications from this drug occur with sufficient frequency to demand particular attention.[2] The severity of these renal reactions varies greatly; in some instances there occur only small numbers of red cells in the urine and/or ureteral colic or pain in the loins or abdomen; in others there is gross hematuria, oliguria, or anuria with increasing nitrogen retention. Ureteral catheterization has been employed in many instances to remove concretions of sulfadiazine products;[3] there have been several deaths from anuria reported.[4] As the renal complications from sulfadiazine are generally, if not always, due to the precipitation of some form of the drug within the kidney or urinary tract, it seemed that a means of preventing this "chemical" toxic effect might be available. Since the renal complications comprise more than half of the toxic reactions due to this sulfonamide,[5] the safety of therapy with this drug would be much enhanced by prevention of this toxic effect.

We[6] have recently reported briefly laboratory and clinical studies which demonstrate that the administration of appropriate amounts of alkali during oral therapy with 4 to 6 Gm. of sulfadiazine daily prevents crystalluria and renal reactions due to precipitation of drug compounds. This investigation has been extended, and the effect of alkali administration on the prevention of renal complications has also been studied in patients receiving higher dosages of sulfadiazine orally and sodium sulfadiazine intravenously.

From the New York Hospital and Department of Medicine, Cornell University Medical College.

1. Finland, Maxwell; Peterson, O. L., and Goodwin, R. A., Jr.: Sulfadiazine: Further Clinical Studies of Its Efficacy and Toxic Effects in 460 Patients, Ann. Int. Med. **17:** 920 (Dec.) 1942. Dowling, H. F., and Lepper, M. H.: Toxic Reactions Following Therapy with Sulfapyridine, Sulfathiazole and Sulfadiazine, J. A. M. A. **121:** 1190 (April 10) 1943. Flippin, Schwartz and Domm.[20] Plummer and Wheeler.[5]

2. Raines, S. L.: Ureteral Obstruction Following the Use of Sulfadiazine, J. A. M. A. **119:** 496 (June 6) 1942. Finland, Peterson and Goodwin.[1] Flippin, Schwartz and Domm.[20] Dowling and Lepper.[1] Plummer and Wheeler.[5] Bradford and Shaffer.[9] Schulte, Shidler and Niebauer.[21] Hellwig and Reed.[3] Keitzer and Campbell.[9] Jeck and Orkin.[27]

3. Hellwig, C. A., and Reed, H. L.: Fatal Anuria Following Sulfadiazine Therapy, J. A. M. A. **119:** 561 (June 13) 1942. Finland, Peterson and Goodwin.[1] Schulte, Shidler and Niebauer.[21] Raines.[2] Jeck and Orkin.[27]

4. Finland, Peterson and Goodwin.[1] Bradford and Shaffer.[9] Hellwig and Reed.[3] Jeck and Orkin.[27]

5. Plummer, Norman, and Wheeler, Charles: To be published.

6. Gilligan, Dorothy Rourke; Garb, Solomon, and Plummer, Norman: Prevention of Crystalluria During Sulfadiazine Therapy: Experimental and Clinical Studies, Proc. Soc. Exper. Biol. & Med. **52:** 248 (March) 1943.

COMPOSITION AND SOLUBILITIES OF THE URINARY PRECIPITATES FROM SULFADIAZINE

Composition of Precipitates.—Analyses by the Bratton and Marshall[7] method showed that the urinary crystals and small stones from the kidney pelves of 8 patients receiving sulfadiazine orally were chiefly acetylsulfadiazine[8] (table 1). These results confirm reported analyses of stones from 3 other patients treated with sulfadiazine.[9] The crystals from 1 of our patients (3, table 1) who received the drug orally were positively identified with the polarizing microscope and were chiefly acetylsulfadiazine.[10] It is of interest that the urinary crystals from 1 of 3 patients who were being treated with 5 Gm. daily of sodium sulfadiazine intravenously were found to consist largely of free sulfadiazine (table 1).

A study of the solubility in buffer solutions of the urinary crystals from 1 patient showed a solubility curve (chart 1) similar to that of pure acetylsulfadiazine (chart 2).

Solubilities of Sulfadiazine and N_4-Acetylsulfadiazine in Buffers and in Normal Urine.—The solubilities of both sulfadiazine and acetylsulfadiazine[11] in phosphate and citrate buffer solutions increase greatly with increasing p_H over the physiologic range of urinary p_H.[12]

TABLE 1.—*Composition of Urinary Crystals from Patients Receiving Sulfadiazine* *

Patient	Route of Sulfadiazine Medication	Composition of Crystals: Sulfadiazine, per Cent	Composition of Crystals: Acetylsulfadiazine, per Cent
1	Oral	7	93
2	Oral	13	87
3	Oral	5	95
4	Oral	13	87
5	Oral	37	63
6	Oral	10	90
7	Oral	6†	94
8	Oral	4†	95
9	Intravenous	10	90
10	Intravenous	12	88
11	Intravenous	78	22

* The urinary sediments from centrifugation were washed once with distilled water. From 70 to 100 per cent (average 90 per cent) of the weight of the sediments consisted of sulfadiazine compounds.
† These specimens were small stones from kidney pelves at autopsy.

(chart 2). When sulfadiazine and acetylsulfadiazine are dissolved together in phosphate buffers of varying p_H's the solubility curve for each solute is the same as that obtained when the compounds are dissolved separately. Curves of solubility identical to those obtained with buffers (chart 2) were obtained from a study of 25 aliquot samples (adjusted to varying p_H levels) of urine from 5 normal subjects. Rose, Martin and

7. Bratton, A. C., and Marshall, E. K., Jr.: A New Coupling Component for Sulfanilamide Determination, J. Biol. Chem. **128:** 537 (May) 1939.

8. Throughout this paper the N_4-acetyl derivatives of the sulfonamides are referred to simply as the "acetyl" derivative.

9. Bradford, H. A., and Shaffer, J. H.: Renal Changes in a Case of Sulfadiazine Anuria, J. A. M. A. **119:** 316 (May 23) 1942. Keitzer, W. A., and Campbell, J. A.: Renal Complications of Sulfadiazine, ibid. **119:** 701 (June 27) 1942.

10. Dr. E. F. Williams of American Cyanamid Company, Inc., made this examination.

11. These compounds were supplied to us by Lederle Laboratories, Inc.

12. The solubility data in buffers[6] and in urine were obtained by shaking an excess of the compound in the buffer or urine sample for eighteen hours at 37 C., filtering at the same temperature, measuring the p_H of the filtrate with a Beckman glass electrode p_H meter and determining the amount of compound dissolved by the Bratton and Marshall method.[7] It was established that equilibrium was reached in eighteen hours both in buffers and in urines by comparing findings after eighteen and forty-two hours of shaking. This method of study does not allow "supersaturation," which Jensen and Fox[13] found complicated their studies of the solubility of these sulfonamides in urine.

Bevan [13] and Jensen and his co-workers [14] also recently reported curves showing increasing solubility of these compounds with increasing p_H in water plus varying amounts of sodium hydroxide [13] and in normal urine.[15]

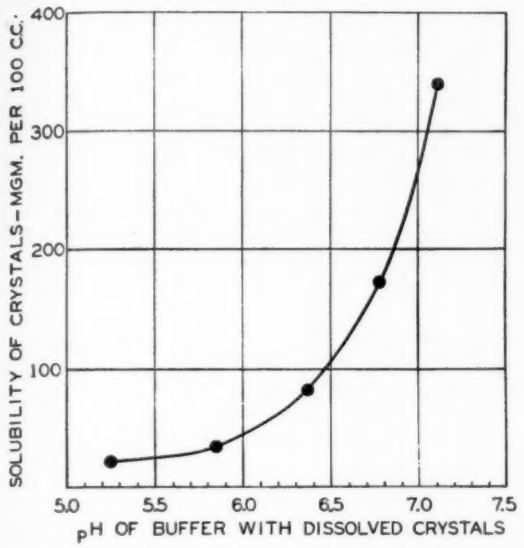

Chart 1.—The solubility in fifteenth molar phosphate buffers of the urinary crystals from a patient receiving sulfadiazine. The values plotted represent the solubility of the acetylsulfadiazine component, which was 93 per cent of the total crystal weight.

As shown in chart 1, sulfadiazine is approximately twenty times, and acetylsulfadiazine thirty times, more soluble in buffers and in normal urine at p_H 7.5 than at p_H 5.0. In fact, at neutrality (p_H 7.0) sulfadiazine is approximately seven times and acetylsulfadiazine thirteen times more soluble than at p_H 5.0 (chart 2).

CLINICAL STUDIES OF THE PREVENTION OF CRYSTALLURIA AND RENAL REACTIONS DURING SULFADIAZINE THERAPY

From the facts that the precipitated products causing the renal toxicity from sulfadiazine in man are acetylsulfadiazine and, less frequently, free sulfadiazine (table 1) and that the solubilities of these compounds are much higher at p_H 7.0 and above than at p_H 5.0 to 6.0 (chart 2), it seemed likely that the maintenance of a neutral to slightly alkaline urine might prevent renal reactions during sulfadiazine therapy.

Studies of Patients Receiving the Usual Oral Dosages of Sulfadiazine.—In a carefully controlled study of the incidence of crystalluria in acid and alkaline urines from 73 patients receiving 4 to 6 (usually 6) Gm. daily of sulfadiazine and varying amounts of sodium bicarbonate, crystals were found in 27 per cent of 172 acid specimens and in only 1.4 per cent of 147 neutral or alkaline specimens [16] (table 2).[6] Factors other than p_H which might affect the incidence of crystalluria, namely the average daily urinary volume, the average specific gravity of the urine specimen examined and the average daily dose of sulfadiazine, were essentially the same in the two groups. The urines examined were almost always the first specimens voided in the morning and were not refrigerated. These specimens were considered most appropriate for study since they are generally the most concentrated and most acid of the day. The daily urinary volume was usually between 1,200 and 2,500 cc.; the specific gravity of the urine specimens examined was generally from 1.006 to 1.016. Twelve patients who had had crystalluria in acid specimens no longer had crystals after sufficient sodium bicarbonate was administered to render the urine neutral or alkaline. In 2 patients showing crystals in acid urines, crystals were still present on the first morning the urines were rendered alkaline by alkali therapy but were absent subsequently during the maintenance of alkaline urines. These two are the only instances in which crystals were observed in alkaline urine (table 2). It is suggested that these crystals were formed when the urine was acid and were being washed out of the urinary tract subsequently. On the other hand, we have observed gross crystalluria disappear in the first urine voided a few hours after the ingestion of 6 Gm. of sodium bicarbonate. It is significant that crystalluria was observed frequently in acid urines of low specific gravity (1.006 to 1.010) as well as in acid urines of higher specific gravity.

Although renal complications result from precipitation of sulfadiazine compounds, it is not implied that the presence of rare or even gross crystalluria necessarily indicates the presence of renal complications. In fact, the incidence of crystalluria (approximately 30 per cent) in patients not treated with adjuvant alkali therapy is much higher than the incidence of discernible renal irritation or urinary tract obstruction (4.8 per cent [5]) in patients similarly treated.

In a series of 350 patients treated to date in the various services of the hospital with 6 Gm. orally of sulfadiazine per day and sufficient alkali to maintain the urine neutral or alkaline throughout the sulfadiazine therapy, there have been no instances of crystalluria and no evidence of renal irritation or urinary tract

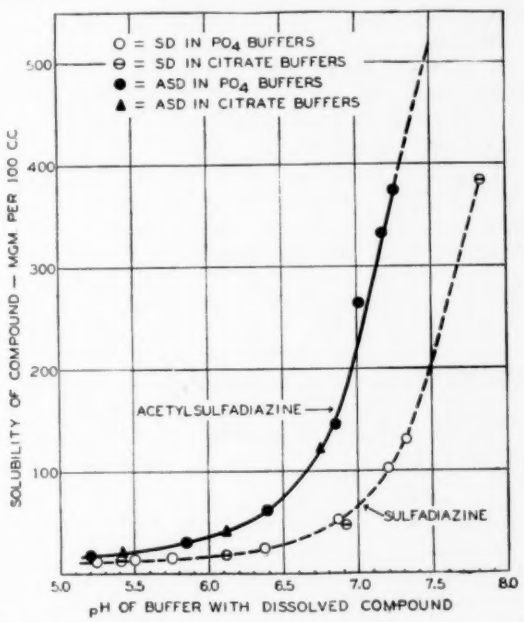

Chart 2.—The curves of solubility of sulfadiazine and of acetylsulfadiazine in fifteenth molar phosphate and in tenth molar citrate plus sodium hydroxide buffer solutions of varying p_H values.

13. Rose, F. L.; Martin, A. R., and Bevan, H. G. L.: Sulfamethazine (2-4'-Aminobenzene-sulfonylamino-4: 6-Dimethylpyrimidine), a New Heterocyclic Derivative of Sulfanilamide, J. Pharmacol. & Exper. Therap. **77:** 127 (Feb.) 1943.

14. Fox, C. L., Jr.; Jensen, O. J., Jr., and Mudge, G. H.: Prevention of Renal Obstruction During Sulfadiazine Therapy, J. A. M. A. **121:** 1147 (April 3) 1943. Jensen and Fox.[15]

15. Jensen, O. J., Jr., and Fox, C. L., Jr.: Hydrogen Ion Concentration and the Solubility of Sulfonamides in Urine: The Relation to Renal Precipitation, J. Urol. **49:** 334 (Feb.) 1943.

16. The urinary p_H values in these studies were estimated with nitrazine paper and frequently checked by measurement with the Beckman glass electrode p_H meter. In particular instances when indicated the fresh urine specimens were immediately placed under toluene and the p_H determined shortly thereafter with the Beckman p_H meter.

obstruction attributable to the drug. The importance of these findings is obvious when compared with the incidence of approximately 30 per cent crystalluria (table 3) and 4.8 per cent of mild to more severe renal complications [5] encountered in this hospital prior to the use of adjuvant alkali therapy.

Studies of Patients Receiving Large Oral Doses of Sulfadiazine.—The effect of adjuvant alkali therapy has been studied in 9 patients [17] receiving orally 12 to 15 Gm. of sulfadiazine daily for periods of several weeks to months. The blood sulfadiazine levels were from 12 to 25 mg. per hundred cubic centimeters. The daily urinary volumes ranged from 1,000 to 3,000 cc. The total daily sulfadiazine excretion in the urine ranged from 9 to 14 Gm. Over 100 urine specimens from this group of patients were examined.

TABLE 2.—*Effect of Urinary p_H on Incidence of Crystalluria from Sulfadiazine in 73 Patients Receiving 4 to 6 Gm. of Sulfadiazine Orally per Day With or Without Varying Doses of Sodium Bicarbonate*

	Acid Urines	Neutral or Alkaline Urines
Number of specimens	172	147*
Number of specimens with crystals	47	2
Percentage of specimens with crystals	27†	1.4

* 132 of these 147 urine specimens were from patients receiving alkali therapy.
† Some of these urines were from patients receiving small amounts of sodium bicarbonate, which accounts for the somewhat lower incidence of crystalluria in this analysis than in that of table 3 for patients receiving no alkali. The degree of crystalluria varied from rare crystals detected by microscopic study of several fields of the smeared, covered sediment to "gross" crystalluria.

Although the incidence of renal complications in patients receiving such large dosages of sulfadiazine is very high when no adjuvant alkali therapy is given, none of these 9 patients showed crystalluria or any evidences of renal complications when the urines were maintained alkaline with 19.5 Gm. of sodium bicarbonate daily in divided doses of 3.25 Gm. (50 grains) every four hours. In 1 of these patients (L. C.) on two occasions during three months of therapy with 15 Gm. of sulfadiazine and 19.5 Gm. of sodium bicarbonate per day the alkali therapy was discontinued in order to ascertain with certainty its value. On both occasions crystalluria occurred when the urines became acid. On the first occasion there developed, shortly after the omission of alkali, pain in the loins with gross hematuria, which disappeared on resumption of alkali therapy; on the second occasion the alkali therapy was promptly resumed when acid urines with crystalluria and microscopic hematuria were voided. Similarly, in another of these patients (J. O.) receiving high dosages of sulfadiazine, gross crystalluria, microscopic hematuria and pain in the loins occurred on one occasion when the adjuvant alkali therapy was temporarily interrupted.

Studies of Patients Receiving 5 Gm. Daily of Sodium Sulfadiazine Intravenously.—In a study of 61 urine specimens from 23 patients receiving daily 5 Gm. of sodium sulfadiazine intravenously in two doses of 2.5 Gm. each and no adjuvant alkali therapy, most of the urines were found to be acid and the incidence of crystalluria was 43 per cent. These were surgical patients receiving intravenous sodium sulfadiazine therapy for approximately two to four days. All the urines containing crystals were acid. It is to be noted that the incidence of crystalluria in this group was appreciably higher than in patients receiving 6 Gm. of sulfadiazine orally per day and no adjuvant alkali therapy (table 3). In 2 patients not included in the foregoing series, 1,000 cc. of sixth molar sodium lactate solution per day was given intravenously in divided doses adjuvant to sodium sulfadiazine therapy. The urines of these patients were alkaline and there was no crystalluria.

The Appropriate Dosage of Adjuvant Alkali Therapy.—The dosage of sodium bicarbonate necessary to maintain the urine neutral or slightly alkaline is variable, of course, in different patients. When alkalis are not administered, the urines of patients receiving sulfadiazine are almost always acid, usually from p_H 5.0 to 6.0. This acidity is to be expected in part on the basis of the usual acidity of the urine in infection and in part because of the acidifying effect of the drug and its derivatives excreted in the urine. The acidifying effect of this sulfonamide is exemplified by our finding that the solution of 136 mg. of sulfadiazine per hundred cubic centimeters decreased the p_H of fifteenth molar phosphate buffer from 7.67 to 7.32. It is to be noted in this respect that the average concentrations in the urine of sulfadiazine and of acetylsulfadiazine are approximately 200 and 100 mg. per hundred cubic centimeters respectively when the daily urine volume is 1,500 cc. and the dosage of sulfadiazine 6 Gm. per day.

The effects of 6 to 19.5 Gm. of sodium bicarbonate daily on the urinary p_H and incidence of crystalluria were studied in 40 patients and the findings compared with those in 23 patients receiving no adjuvant alkali therapy (table 3). An initial dose of 4 to 6 Gm. of sodium bicarbonate was administered at the beginning of sulfadiazine therapy, and the daily doses were divided into six equal parts administered every four hours together with the sulfadiazine. Urine specimens known to contain urea splitting organisms were excluded from the analysis.

With doses of 6 to 12 Gm. (average 8 Gm.) daily of bicarbonate, the incidence of acid urines and of crystalluria was reduced only about one third (table 3).

TABLE 3.—*Study of Bicarbonate Dosage Required to Maintain Urine Neutral to Alkaline in Patients Receiving 4 to 6 Gm. (Usually 6 Gm.) of Sulfadiazine Orally per Day*

Daily Dosage of Sodium Bicarbonate, Gm.	Number of Patients	Number of Urines	Per Cent of Crystalluria*	Per Cent of Acid Urines
0	23	90	31	90
8†	13	71	18	59
13.7	10	39	0	15
19.5	17	51	0	0

* All the crystals were observed in acid urines.
† Average dosage in 13 patients receiving 6 to 12 Gm. daily.

One patient in this group, who was receiving 12 Gm. of alkali daily and who showed acid urines with crystalluria, developed gross hematuria. With 13.7 Gm. of bicarbonate daily (six doses of 35 grains) the urines were usually neutral or alkaline, although 15 per cent were between p_H 6.3 and 6.8. With 19.5 Gm. daily (six doses of 50 grains) all the urines were alkaline. In both of these latter groups there was no crystalluria and no gross or microscopic hematuria. These doses of alkali were well tolerated; none of the patients had gastrointestinal symptoms and there were no clinical evidences of alkalosis. One patient who received 12 to 15 Gm. of sulfadiazine daily for the treatment of sub-

17. Five of these patients were being treated for subacute bacterial endocarditis.

acute bacterial endocarditis also received 19.5 Gm. of sodium bicarbonate daily for three months without showing intolerance to this medication.

COMMENT

Some other investigators have previously advocated adjuvant alkali therapy with sulfadiazine medication on the basis of their clinical findings.[18] Schwartz and his collaborators [19] reported a slight reduction in the incidence of crystalluria from oral sulfadiazine therapy in patients receiving sodium bicarbonate in amounts equal to the sulfadiazine.[20] The failure of the alkali therapy to produce a significant lowering of the incidence of crystalluria in this series [19] can be attributed to the inadequate dosage of alkali, as evidenced by our findings. Fox, Jensen and Mudge [14] more recently have reported 2 cases of subacute bacterial endocarditis in which alkalis were used in conjunction with massive doses of intravenous sodium sulfadiazine. In these 2 cases complete anuria did not develop although renal reactions of less severity occurred; the authors [14] point out that in these cases the amounts of alkali administered were insufficient to maintain the urines alkaline during the period of therapy and that precipitation occurred when the urines were acid. Schulte, Shidler and Niebauer [21] reported a case of acute urinary suppression following sulfadiazine therapy in which urinary flow was reestablished following oral alkali therapy and lavage of the kidney pelves with 2 per cent sodium bicarbonate solution.

The present studies, carried out on a large series of patients, showed that appropriate adjuvant alkali therapy prevented crystalluria, clinical evidences of renal damage and urinary tract obstruction from sulfadiazine therapy. This protection applied to patients receiving the usual therapeutic doses of sulfadiazine orally, large doses of sulfadiazine orally and the usual doses of sodium sulfadiazine intravenously. The clinical study of the effect of adjuvant alkali therapy was prompted by the chemical studies, which demonstrated that the precipitate which caused the renal reactions was usually chiefly composed of acetylsulfadiazine [22] (table 1) or, under particular circumstances, free sulfadiazine (table 1) and that the solubility of these pure compounds (chart 2) and of the urinary crystals (chart 1) was definitely greater at p_H 7.0 and above than at the usual acidity of the urine of patients receiving sulfadiazine.

That fluids should be administered during sulfonamide therapy in quantities sufficient to maintain large daily urinary volumes is generally accepted and has been widely advocated. It has further been shown repeatedly that severe renal reactions due to sulfonamide therapy are much more frequent in patients in whom the daily urinary volumes have been low during treatment with the drugs. The frequency with which mild or more severe renal reactions occur during treatment with sulfonamides in hospital patients on a regimen of carefully controlled therapy,[1] however, attests the fact that a feasible routine of fluid therapy is insufficient to prevent the occurrence of such reactions. That renal reactions occur during therapy with the usual daily doses of sulfadiazine or sodium sulfadiazine, even when daily urinary volumes of approximately 1,500 cc. have been maintained, has been pointed out by Plummer and Wheeler.[5] In patients receiving larger doses of sulfadiazine without adjuvant alkali therapy the frequency of renal reactions is extremely high in spite of maximal fluid intake compatible with the comfort of the patient. It may also be pointed out that under certain circumstances, especially those incumbent on war operations today, sulfonamide therapy may be required under conditions in which amounts of fluid sufficient to afford more than a scanty urinary volume are not available. It is to be noted also that acidosis is often associated with dehydration. The remarkable effectiveness of an alkaline urine as a safeguard against renal reactions is a consequence of the fact that sulfadiazine is some twenty times, and acetylsulfadiazine some thirty times, more soluble at p_H 7.5 than at p_H 5.0 (chart 2).

From the results of studies with varying daily dosages of alkali, it has been concluded that adjuvant therapy consisting of an initial 6 Gm. dose of sodium bicarbonate followed by a daily amount of 15.6 Gm. divided into 2.6 Gm. (40 grain) doses administered every four hours is generally adequate to prevent crystalluria and renal reactions during oral therapy with 6 Gm. of sulfadiazine. The dosage of alkali is increased or decreased in an individual patient when indicated by clinical or laboratory findings. The urinary p_H may be tested simply with litmus or nitrazine paper, both of which indicators are blue in neutral and alkaline urines. The prescribed amount of 15.6 Gm. of bicarbonate daily is conservative and is based on studies of patients in the Isolation Service of the New York Hospital (table 3). Twenty-four Gm. of sodium bicarbonate daily has been administered routinely for short periods to obstetric patients receiving 6 Gm. daily of sulfadiazine with no apparent ill effects [23] and no increase above normal in the carbon dioxide combining power of the plasma. It is necessary that the alkali be given in divided doses every four hours in order to maintain the urinary p_H relatively constant throughout the day and night. Alkali therapy is continued for one day following cessation of sulfadiazine therapy. The same dosage of alkali should be used for patients receiving 4 Gm. of sulfadiazine daily. Since microscopic hematuria and pain in the loins sometimes occurs in ambulatory patients receiving 3 Gm. of sulfadiazine daily,[5] adjuvant alkali therapy should probably also be employed even with these small doses of sulfadiazine. We have employed the daily dosage of 19.5 Gm. of bicarbonate in patients receiving 12 to 15 Gm. of sulfadiazine by mouth daily. It should be noted that in patients with urinary tract infections with urea splitting organisms the voided urine may be strongly alkaline as

18. Flippin, Schwartz and Domm.[20] Schulte, Shidler and Niebauer.[21] Fox, Jensen and Mudge.[14] Schwartz, Flippin, Reinhold and Domm.[19]

19. Schwartz, Leon; Flippin, H. F.; Reinhold, J. G., and Domm, A. H.: The Effect of Alkali on Crystalluria from Sulfathiazole and Sulfadiazine, J. A. M. A. **117:** 514 (Aug. 16) 1941.

20. Flippin, H. F.; Schwartz, Leon, and Domm, A. H.: Modern Treatment of Pneumococcic Pneumonia, J. A. M. A. **121:** 230 (Jan. 23) 1943. Schwartz, Flippin, Reinhold and Domm.[19]

21. Schulte, J. W.; Shidler, F. P., and Niebauer, J. J.: Acute Urinary Suppression Following Sulfadiazine Therapy, J. A. M. A. **119:** 411 (May 30) 1942.

22. That urinary crystals from sulfapyridine and sulfathiazole are chiefly the acetyl derivatives [30] of the drugs agrees with the observation that these derivatives are less soluble than are the free drugs (table 4). It has not been appreciated by many investigators, however, that the urinary precipitates from oral sulfadiazine therapy are generally composed chiefly of acetylsulfadiazine. This finding appears at first paradoxical, since the true solubility of acetylsulfadiazine in buffers and in normal urine is greater than that of sulfadiazine (chart 1), and since the concentration of this derivative in the urine of patients receiving the drug is usually less than half that of the free drug (Plummer, Norman, and Ensworth, H. K.: Absorption and Excretion of Sulfadiazine, Proc. Soc. Exper. Biol. & Med. **45:** 734 [Nov.] 1940) and cannot be completely explained until further knowledge is available concerning the state of solution of the urinary excretory products during sulfadiazine therapy. This problem is receiving study in this laboratory (Gilligan, Dorothy Rourke, and McDermott, Walsh: To be published). That free sulfadiazine would precipitate after intravenous injections of large amounts of sodium sulfadiazine intravenously is understandable.

23. Dr. R. Gordon Douglas analyzed these cases.

the result of ammonia production; nevertheless alkali therapy is still indicated in order to maintain the appropriate p_H in the urine in the tubules.

Since intravenous therapy with sodium sulfadiazine in amounts of 5 Gm. per day occasions a particularly high incidence of crystalluria and of renal complications,[5] adjuvant alkali therapy is obviously indicated with such a regimen even though it should be necessary to administer the alkali by the intravenous route. The sodium sulfadiazine itself provides an insignificant amount of alkali, since 5 Gm. of this drug has the sodium content (0.42 Gm.) of only 1.5 Gm. of sodium bicarbonate.

Loughlin and his collaborators [24] have recently shown that the blood level of sulfadiazine rises approximately twice as fast when 4 Gm. of sodium bicarbonate is given orally together with a single 4 Gm. dose of sulfadiazine as when the sulfadiazine is given alone. This advantage of increasing the blood level more rapidly would apply when the initial dose of 6 Gm. of bicarbonate is given, as prescribed at the onset of therapy with sulfadiazine. The data of these authors [24] show a considerably higher percentage of acetylation of the sulfadiazine in the blood when bicarbonate was given with a single dose of sulfadiazine than when sulfadiazine was given alone. Daily blood and urine studies made by us on a group of patients receiving daily adjuvant alkali therapy showed no higher percentage of acetylation of the sulfadiazine than when sulfadiazine was given alone.

TABLE 4.—*Solubilities of Various Sulfonamides and of Their N_4-Acetyl Derivatives at Different p_H Levels*

Reference	Compound	Solubility p_H 5.5 Mg./100 Cc.	6.5 Mg./100 Cc.	7.5 Mg./100 Cc.
Macartney, Smith, Luxton, Ramsey and Goldman [31]	Sulfapyridine*	61	61	62
	Acetylsulfapyridine*	33	34	37
Climenko, Barlow and Wright: Arch. Path. **32**: 880 (Dec.) 1941	Sulfathiazole	98	108	235
	Acetylsulfathiazole	7	9	28
Chart 2	Sulfadiazine	13	28	200
	Acetylsulfadiazine	20	75	512
Gilligan and Plummer: Comparative Solubilities of Sulfadiazine, Sulfamerizine and Sulfamethazine and Their N_4-Acetyl Derivatives at Varying p_H Levels, Proc. Soc. Exper. Biol. & Med., **53**: 142 (June) 1943	Sulfamerizine	35	45	170
	Acetylsulfamerizine	38	57	272
	Sulfamethazine	69	76	140
	Acetylsulfamethazine	90	107	240

* Solubilities in water plus varying amounts of sodium hydroxide. All other solubilities measured in buffers.

Alkalosis should not be encountered during the regimen of adjuvant alkali therapy that has been outlined, since it has been shown that only sufficient alkali need be administered to maintain the urine neutral to slightly alkaline, whereas the normal kidney has the capacity of excreting alkali sufficient to produce a urinary p_H of 8.2.[25] Bischoff [26] has demonstrated that 30 Gm. of sodium citrate daily is the minimum dosage of alkali which produces a shift in the acid base equilibrium of the plasma outside the normal variation of the normal individual. In a series of patients studied here who received as much as 24 Gm. of sodium bicarbonate together with 6 Gm. of sulfadiazine daily, the plasma bicarbonate values were all within the limits of normal.

In some instances, such as in cardiac or renal insufficiency, adjuvant sodium bicarbonate therapy may be contraindicated. However, the incidence of severe renal reactions in such conditions during sulfadiazine treatment without appropriate fluid and alkali therapy is very high.[27] It would seem that the seriousness of a possible severe renal reaction from sulfadiazine would outweigh the danger of increasing edema by adjuvant therapy with fluid and alkali in a patient with cardiac decompensation during a short period of treatment for an acute infection. It may be that a potassium salt of an organic acid can be used in place of a sodium salt in cardiac patients; however, increased potassium in the blood has been shown experimentally to produce cardiac arrhythmias.[28] The same caution must be exercised in the administration of alkalis as in the administration of the sulfonamides for patients with renal insufficiency.

Sodium lactate or sodium citrate may be preferred to sodium bicarbonate for adjuvant alkali therapy. These former salts do not act as alkalis in the alimentary tract and therefore should be substituted for sodium bicarbonate for any patient in whom the latter salt causes gaseous eructations, nausea or a purgative effect. The dosage of sodium lactate is one third greater and that of sodium citrate ($Na_3C_6H_5O_7 2H_2O$) approximately one fifth greater than that of sodium bicarbonate; i. e., 20.8 Gm. of sodium lactate or 18.2 Gm. of sodium citrate afford an equivalent alkali excess to that of 15.6 Gm. of sodium bicarbonate. Sterile, isotonic (sixth molar) sodium lactate solution affords a means of giving alkalis intravenously. One hundred cc. of this solution (sixth molar) is equivalent to 1.4 Gm. of sodium bicarbonate.

That crystalluria is rarely [29] encountered during therapy with sulfanilamide is attributable to the greater solubilities of this drug and its acetyl derivative compared with sulfapyridine, sulfathiazole and sulfadiazine and their acetyl derivatives. Investigation of the value of adjuvant alkali therapy in preventing renal complications from sulfadiazine would perhaps have been made much earlier if it had not been common clinical experience that alkali therapy was of no value in preventing renal complications from sulfapyridine. The explanation for this failure is now known to reside in the solubility characteristics of sulfapyridine and its acetyl derivative; there is no increase in their solubility with increasing p_H within the physiologic range of urinary p_H (table 4), whereas sulfadiazine and acetylsulfadiazine are much more soluble in the alkaline than in the acid range of urinary p_H. Schwartz and his collaborators [19] have reported a significantly lower incidence of crystalluria from sulfathiazole when sodium bicarbonate was administered in equal doses to those of the drug than when sulfathiazole was given without alkali. Further clinical studies on the prevention of renal complications from sulfathiazole with larger doses of alkali

24. Loughlin, E. H.; Bennet, R. H.; Flanagan, Mary E., and Spitz, S. H.: Relative Absorption and Conjugation of Nine Compounds by Humans During a Three-Hour Period (Free and Conjugated Blood Level Determinations During a Three-Hour Period Following Peroral Administration of the Acid Salts Alone, the Acid Salts with Sodium Bicarbonate and the Sodium Salts of Sulfapyridine, Sulfathiazole and Sulfadiazine), Am. J. M. Sc. **205**: 223 (Feb.) 1943.

25. Gamble, J. L.: Carbonic Acid and Bicarbonate in Urine, J. Biol. Chem. **51**: 295 (March) 1922.

26. Bischoff, Fritz; Sansum, W. D.; Long, M. Louisa, and Dewar, Margaret M.: The Effect of Acid Ash and Alkaline Ash Foodstuffs on the Acid-Base Equilibrium of Man, J. Nutrition **7**: 51 (Jan.) 1934.

27. Jeck, H. S., and Orkin, Lazarus: Toxic Renal Reactions Following the Use of Sulfadiazine, J. Urol. **49**: 290 (Feb.) 1943.

28. Nahum, L. H., and Hoff, H. E.: Observations on Potassium Fibrillation, J. Pharmacol. & Exper. Therap. **65**: 322 (March) 1939.

29. Stewart, J. D.; Rourke, G. M., and Allen, J. G.: Excretion of Sulfanilamide, J. A. M. A. **110**: 1885 (June 4) 1938.

have not to our knowledge been published. The solubility in buffers of acetylsulfathiazole, of which the urinary crystals are composed,[30] increases only from 7 mg. per hundred cubic centimeters at p_H 5.5 to 28 mg. per hundred cubic centimeters at p_H 7.5, whereas the solubility of acetylsulfadiazine increases from 20 mg. per hundred cubic centimeters at p_H 5.5 to 512 mg. per hundred cubic centimeters at p_H 7.5. Two substituted sulfadiazine compounds, sulfamerizine and sulfamethazine, are at present receiving clinical study in this country and abroad;[31] these clinical studies have been prompted largely by the greater solubilities of these substituted sulfadiazine compounds and of their acetyl derivatives than of sulfadiazine and acetylsulfadiazine in the acid range of urinary p_H (table 4).

CONCLUSIONS

1. The urinary precipitate which causes renal complications and obstruction to urinary flow during oral sulfadiazine therapy usually consists chiefly of acetylsulfadiazine. Free sulfadiazine sometimes precipitates in the urine after intravenous sodium sulfadiazine.

2. The urine is almost always acid (usually p_H 5.0 to 6.0) in patients receiving sulfadiazine without adjuvant alkali therapy. With minor exceptions, crystalluria from sulfadiazine is found only in acid urines.

3. The solubilities of sulfadiazine and of acetylsulfadiazine in buffers and in urine increase a great deal with increasing p_H within the physiologic range of urinary p_H. The amounts of sulfadiazine and of acetylsulfadiazine dissolved in a given volume of buffer solution or normal urine at p_H 7.5 are approximately twenty and thirty times respectively the amounts dissolved at p_H 5.0.

4. Crystalluria and evidences of renal damage or of urinary tract obstruction were not encountered in 350 patients in whom the urine was maintained neutral or alkaline by adjuvant alkali therapy during treatment with 6 Gm. daily of sulfadiazine or in smaller groups of patients receiving twice this dosage of sulfadiazine orally or sodium sulfadiazine intravenously.

5. On the basis of clinical studies, 15.6 Gm. daily of sodium bicarbonate (or amounts of other organic sodium salts with equivalent available base excess), divided into six doses of 2.6 Gm. (40 grains) administered every four hours, is recommended as the dosage usually appropriate to maintain the urine neutral or slightly alkaline during sulfadiazine therapy in adults. Regimens of alkali therapy for patients receiving unusually large doses of sulfadiazine orally or sodium sulfadiazine intravenously have also been adopted. A sufficient volume of fluid should be given to provide a daily urinary output of 1,500 cc. or more.

6. The findings of these laboratory and clinical studies lead to the conclusion that renal damage and urinary tract obstruction consequent to precipitation of sulfadiazine and acetylsulfadiazine are preventable and that adjuvant alkali therapy sufficient to maintain the urine neutral or slightly alkaline should be prescribed whenever sulfadiazine is administered.

30. Prien, E. L., and Frondel, Clifford: Crystallography of the Urinary Sediments with Clinical and Pathological Observations in Sulfonamide Drug Therapy, J. Urol. **46**: 748 (Oct.) 1941.

31. Macartney, D. W.; Smith, G. S.; Luxton, R. W.; Ramsey, W. A., and Goldman, Jacob: Sulfamethazine: Clinical Trial of a New Sulfonamide, Lancet **1**: 639 (May 30) 1942. Jennings, P. A., and Patterson, W. H.: Sulfamethazine: Clinical Trials in Children, ibid. **2**: 308 (Sept. 12) 1942. Goodwin, R. A., Jr.; Peterson, O. L., and Finland, Maxwell: Absorption and Excretion of Sulfamethyldiazine (2-sulfanilamido-4-methylpyrimidine) in Human Subjects, Proc. Soc. Exper. Biol. & Med. **51**: 262, 1942.

THE PRODUCTION OF DIABETES MELLITUS IN RABBITS WITH ALLOXAN

A PRELIMINARY REPORT

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In 1937 Jacobs[1] found that alloxan[2] (the ureide of mesoxalic acid) produced fatal hypoglycemia when injected intravenously into rabbits. No histologic observations were recorded. Similar experiments conducted by Dunn, Sheehan and McLetchie[3] confirmed the hypoglycemic action of alloxan. On microscopic study these observers found necrosis of all the islets of Langerhans while the acinar tissue escaped injury. All but 1 of their animals died apparently in hypoglycemia.

If alloxan produces extensive necrosis of the islets of Langerhans without apparent damage to the acinar tissue and relatively minor changes in other organs, it seemed to us that the hypoglycemic phase might be transitory. Should this be true, animals kept alive by repeated injections of dextrose might survive this phase and finally develop diabetes mellitus. A series of experiments designed to test this hypothesis has shown that such is the case. Six 3 months old male Dutch rabbits were used. Each received intravenously 200 mg. of alloxan per kilogram of body weight. The injection was made in three equal parts over a period of forty-five minutes. Blood sugars were determined every fifteen minutes for the first two or three hours and at hourly intervals thereafter. The rabbits were observed constantly for sixteen to twenty-four hours, and 50 per cent dextrose was given intravenously whenever hypoglycemic convulsions occurred. Frequent rectal temperatures were recorded and the clinical condition of the rabbits was constantly watched.

After the first twenty-four hours some of the animals were placed in metabolism cages where water intake and urine output and urinary sugar could be accurately followed. All of the animals have been under close observation, and frequent blood sugars and nonprotein nitrogens[4] have been determined.

Our results fully confirm the findings of Jacobs[1] and of Dunn, Sheehan and McLetchie[3] in regard to the initial transitory hyperglycemia lasting approximately one hour immediately after injection of the material and followed by severe hypoglycemia with convulsions. In less than twenty-four hours the hypoglycemic stage had ended, leaving the animals with severe diabetes mellitus, which has persisted in 5 of the 6 animals during a period of two weeks' observation. During this period blood sugar levels have ranged from 360 to 700 mg. per

Mrs. Rachel Smith Leech supervised the chemical analyses and gave valuable technical help. Miss Virginia Kent assisted in the chemical determinations.

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1. Jacobs, H. R.: Hypoglycemic Action of Alloxan, Proc. Soc. Exper. Biol. & Med. **37**: 407 (Nov.) 1937.

2. Alloxan is a component of the uric acid molecule and can be obtained by the oxidation of uric acid with nitric acid. The alloxan used in these experiments was kindly prepared and given us by the American Cyanamid Company.

3. Dunn, J. Shaw; Sheehan, H. L., and McLetchie, N. G. B.: Necrosis of Islets of Langerhans Produced Experimentally, Lancet **1**: 484 (April 17) 1943; Experimental Selective Necrosis of the Islands of Langerhans, editorial, J. A. M. A. **122**: 676 (July 3) 1943.

4. Folin, Otto: Micro Method for the Determination of Nonprotein Nitrogen, in Laboratory Manual of Biological Chemistry with Supplement, ed. 5, New York, D. Appleton-Century Company, Inc., 1934, p. 271.

hundred cubic centimeters; glycosuria has been found up to 10 per cent. Rabbit 3, not given insulin, developed acetonuria and pronounced lipemia (total blood lipids [5] 8,412 mg. per hundred cubic centimeters). The blood acetone [6] (total acetone bodies expressed as acetone) reached 144 mg. per hundred cubic centimeters of blood at the time the animal was killed with air embolism. Rabbit 5 had a blood sugar of 360 mg. per hundred cubic centimeters of blood twenty-four hours after injection. At the end of forty-eight hours the blood sugar returned to normal and has remained so for a period of one week's observation. Rabbits 1 and 6 have received 1 to 4 units of insulin daily to control their diabetes, which has persisted for the total period of observation. Rabbit 2 had been receiving 2 units of insulin daily when it developed severe diarrhea and died on the fourteenth day after injection. Apparently this death was not related to alloxan.

Rabbits 3 and 4 have thus far been killed. In each animal all the cells (both alpha and beta) of all the islets of Langerhans had disappeared completely. No polymorphonuclear leukocytic infiltration was seen. The blood vessels of the islets were preserved and appeared entirely normal. Some of the pancreatic ducts were moderately distended and contained eosinophilic material. Their epithelium, as well as all the acini, showed no changes detectable on microscopic examination. Studies on organs other than the pancreas have not yet been completed.

The following is a representative experiment in the series:

Rabbit 1, weighing 1,520 Gm., was entirely normal during a seven day period of observation. Food was withheld for eighteen hours, at the end of which time two micro blood sugar determinations [7] were 105 and 100 mg. per hundred cubic centimeters. Three hundred and four mg. of alloxan (200 mg. per kilogram of body weight) was then injected intravenously in three divided doses at fifteen minute intervals. Fifteen minutes after the end of the last injection the blood sugar was 208 mg. per hundred cubic centimeters. An hour later it was 105 mg. per hundred cubic centimeters and two and one-half hours after the end of the injection it was 38 mg. per hundred cubic centimeters. The first convulsion developed ten minutes later. Prompt recovery followed the administration of 2 cc. of 50 per cent dextrose intravenously. In the next thirteen hours eleven more hypoglycemic convulsions occurred, each relieved promptly by dextrose intravenously. On the morning after the injection of alloxan the blood sugar was 190 mg. per hundred cubic centimeters and rose to 640 mg. per hundred cubic centimeters on the third day. The rabbit has been kept in good condition for sixteen days by the administration of 2 to 4 units of insulin daily. The amount of insulin required has constantly increased and the blood sugars have varied from 200 to 540 mg. per hundred cubic centimeters. Persistent glycosuria has accompanied the hyperglycemia, the daily dextrose excretion varying between 10 and 22 Gm.[8] Definite polydipsia and polyuria have been observed with water intake ranging between 350 and 700 cc. and urinary excretion between 160 and 470 cc. daily. The body temperature was 104 F. before the experiment was begun and fell to 99 F. at the end of eleven hours but subsequently returned to normal.

Repeated urinalyses have failed to show albuminuria or any abnormal sediments. Blood nonprotein nitrogens [4] have varied from 36.3 to 65.0 mg. per hundred cubic centimeters, whereas normal controls taken prior to the experiments ranged from 42.6 to 60.0 mg. per hundred cubic centimeters.

5. Bloor, W. R.: The Determination of Small Amounts of Lipid in Blood Plasma, J. Biol. Chem. **77:** 53 (April) 1928.
6. Nanavutty, S. H.: Van Slyke's Method of Determination of Acetone Bodies Applied to Small Volumes of Blood and Urine, Biochem. J. **26:** 1391 (No. 5) 1932.
7. Folin, Otto, and Malmros, H.: An Improved Form of Folin's Micro Method for Blood Sugar Determinations, J. Biol. Chem. **83:** 115 (July) 1929.
8. Smith, Millard: A Micromodification of the Method of Benedict for the Quantitative Determination of Reducing Sugar in Urine, J. Lab. & Clin. Med. **7:** 364 (March) 1922.

COMMENT

From these experiments it seems clear that the intravenous administration of alloxan in rabbits in doses of 200 mg. per kilogram of body weight produces an immediate transitory rise in blood sugar followed by hypoglycemia of several hours' duration. If hypoglycemic death is prevented by repeated administration of dextrose an apparently permanent state of hyperglycemia develops within twenty-four hours. Our histologic observations confirm the work of Dunn, Sheehan and McLetchie [3] that selective injury to the islets of Langerhans is produced by alloxan. This is probably the basis for the permanent hyperglycemia. In view of previous work done in this laboratory [9] as well as in other laboratories [10] the initial blood sugar rise, which lasts about one hour, may be similar to a transitory hyperglycemia easily produced in rabbits by the injection of a number of substances. The cause of the prolonged yet limited period (twelve to twenty-four hours) of hypoglycemia which follows is at the present time debatable. Dunn, Sheehan and McLetchie [3] suggest that it may result from a primary stimulation of the islet cells. Another possible explanation may be that necrosis of the islets releases a large amount of insulin. In either case the destruction of the pancreatic islets probably explains the subsequent, apparently permanent, diabetes.

Whatever the mechanism involved, the use of alloxan provides a simple method for the production of diabetes mellitus in rabbits in the laboratory within twenty-four hours. The diabetes mellitus thus induced bears many resemblances to the human disease. There is definite and persistent hyperglycemia and glycosuria with polydipsia and polyuria; the response to insulin is prompt; when insulin is withheld, acetonuria and hyperlipemia may develop. These animals offer acceptable subjects for investigation of many problems of diabetes mellitus as well as in carbohydrate metabolism.

This is a preliminary report, and further studies are being undertaken in regard to the effects of alloxan on various organs as well as the consequences of different dosages of this drug.

SUMMARY

Alloxan when given intravenously to rabbits produces necrosis of the islets of Langerhans. Brief hypoglycemia, if counteracted by repeated injections of dextrose, is followed by the development of symptoms seen in human diabetes, namely hyperglycemia, glycosuria, polydipsia, polyuria, acetonuria and lipemia.

9. Vartiainen, Ilmari, and Marble, Alexander: The Effect of the Subcutaneous Administration of Protamine (Salmine) to Rabbits and Mice, J. Lab. & Clin. Med. **26:** 1416 (June) 1941; Unpublished data.
10. Jensen, Hans; Grattan, J. F., and Hart, G. W.: A Study on the Specificity of the Anti-Insulin Effect, Endocrinology **30:** 203 (Feb.) 1942.

Origin and Nature of Allergy.—The view is now generally accepted that the mechanism of allergic phenomena is based on an antigen-antibody reaction taking place in the cells or tissues. This reaction has also been called the allergen-reagin reaction. Furthermore, it has now been definitely established that neither the antigen (allergen) nor the antibody is in itself the noxious agent and that rather the union of the two initiates the clinical response. The proof of this consists of experiments that have shown that when an organism's supply of antibodies has been depleted renewed exposure to the antigen does not elicit any pathologic changes.—Urbach, Erich, and Gottlieb, Philip M.: Allergy, New York, Grune & Stratton, 1943.

XANTHOMATOSIS

A CAUSE OF CORONARY ARTERY DISEASE IN YOUNG ADULTS

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Though xanthomatosis is but a single manifestation of a systemic pathologic condition, only recently has this disturbance in cholesterol metabolism seriously occupied the attention of any one but the dermatologists. Latterly the occurrence of cardiovascular involvement with cutaneous xanthomatosis has likewise been noted by the internists,[1] but because of the meagerness of the literature on the subject the impression is prevalent that this association is rare. To emphasize the fact that this is not an infrequent occurrence we are presenting 6 cases of xanthomatosis and coronary artery disease that we have seen during the past two years, illustrating their diagnostic features.

REPORT OF CASES

CASE 1.—L. W., a man aged 32, first seen in June 1941, complained of substernal pain on exertion and after heavy meals. The family history revealed that his father had died of a heart attack at 48 and his mother of heart disease at 62. Physical examination was negative except for a small, pinhead size, yellowish papule of the left lower eyelid. The blood pressure was 120/70. The basal metabolic rate was 16 per cent. The Wassermann reaction was negative. An electrocardiogram (fig. 1) was normal at rest but after exercise showed a temporary depression of the ST segment in leads 1, 2 and 4 F. With exercise a typical attack of his substernal pain developed. It was felt that he had coronary insufficiency, and moderation of activity was advised. Four weeks later the patient mentioned that the yellow papule of the eyelid had increased to double its size. He also stated that his younger sister had similar lesions of both eyelids. The blood cholesterol at this time (July 21) was 430 mg. per hundred cubic centimeters and the esters 238 mg. per hundred cubic centimeters. The fasting blood sugar was within normal range. He was placed on a diet low in animal cholesterol. On September 11 the blood cholesterol was 373 mg. per hundred cubic centimeters and the esters 273 mg. per hundred cubic centimeters. During this interval he had symptomatically improved. In December, after unusually severe exertion, he experienced sharp pain in the chest, which persisted for several hours. After this the sedimentation rate became rapid and the abnormal electrocardiographic changes that had been observed only after exercise were now present at rest (fig. 1 *C*). A diagnosis of acute myocardial infarction was made. The patient was kept at bed rest for four weeks and then gradually resumed limited activity. He is now asymptomatic even with moderate exertion. The blood cholesterol in December was 290 mg. and the esters 170 mg. Since the beginning of the diet low in animal cholesterol the xanthoma of the eyelid has not increased in size.

Significant Features.—Familial tendency shown by early cardiac death of the father and xanthomas of the sister's eyelids; normal blood pressure; xanthoma of the skin; onset of angina pectoris at the age of 32; hypercholesteremia with moderate reduction with diet; simultaneous onset of cardiac symptoms and cutaneous lesions.

CASE 2.—N. G., a man aged 48,[2] had an attack of acute coronary thrombosis at the age of 40. In the following five years there were many episodes of severe precordial pain, always initiated by exertion. Examination revealed large masses at each elbow and nodules along the tendons of the hands and feet. According to the patient's story these masses and small nodules along the tendons of the hands and feet had appeared soon after his first cardiac pain. Biopsy of the nodule at the elbow revealed typical xanthomatosis. His blood pressure was 140/90 and the patient definitely stated that on many previous examinations hypertension had never been found. The fasting blood sugar was normal, the blood cholesterol was 275 mg. and the esters 190 mg. per hundred cubic centimeters. Electrocardiograms over several years showed progressive changes with an advanced degree of myocardial damage (fig. 2). One year before admission, six years after the onset of heart disease, he suffered a cerebral accident with paraplegia. Recovery from this has been almost complete. A low cholesterol diet has been maintained for years without decrease in the blood cholesterol and esters.

Significant Features.—Acute coronary thrombosis at 40 years; normal blood pressure; hypercholesteremia with no response on low cholesterol diet; tendon sheath xanthomas, which appeared shortly after the first symptoms of cardiac involvement.

CASE 3.—L. A. W., a man aged 33, first seen in January 1941, complained of episodes of precordial pain on exertion occurring with increasing frequency. His father had died at the age of 40 of acute coronary thrombosis. Examination was

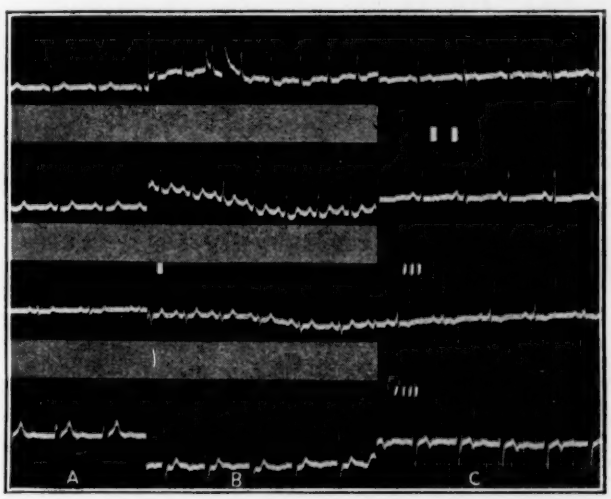

Fig. 1 (case 1).—Tracings made (*A*) at rest, (*B*) immediately after exercise with pain present and (*C*) six days after severe precordial pain of several hours' duration, in December 1941.

completely negative. The blood pressure was 120/80; the urine was normal. One week after the onset of the first anginal episode he suffered a typical attack of acute coronary thrombosis (fig. 3). Recovery was complete, and he has been well ever since. In May 1941, as this paper was being written, it was felt that, in view of the familial story of heart disease at an early age, xanthomatosis might have been the basic condition despite the absence of cutaneous lesions. A blood cholesterol determination done at this time was 305 mg. per hundred cubic centimeters of plasma. The basal metabolic rate was —7 per cent, fasting blood sugar 93 mg.

Significant Features.—Familial history of coronary thrombosis early in life; normal blood pressure; acute coronary thrombosis at the age of 33; hypercholesteremia with absence of cutaneous manifestations of xanthomatosis.

CASE 4.—I. M., a woman aged 48, complained chiefly of attacks of precordial pain on exertion during the past year. Her father had died of heart disease and her mother died

Dr. M. H. Nathanson gave the authors the privilege of following 2 of the cases presented.

From the Departments of Internal Medicine and Dermatology, Cedars of Lebanon Hospital, Los Angeles.

1. Thannhauser, S. J., and Magendantz, Heinz: Ann. Int. Med. **11**: 1662-1746 (March) 1938. Müller, Carl: Angina Pectoris in Hereditary Xanthomatosis, Arch. Int. Med. **64**: 675 (Oct.) 1939.

2. Newman, B. A.: Xanthomatosis with Disease of the Coronary Arteries, Arch. Dermat. & Syph. **45**: 198-199 (Jan.) 1942.

suddenly while doing housework. The patient volunteered the information that she had noticed the appearance of yellow plaques on both eyelids about the time that she had her first attack of pain. Examination was negative except for xanthomatous plaques on the inner portion of all eyelids. Blood pressure varied from 150/80 to 170/90. Fluoroscopy of the

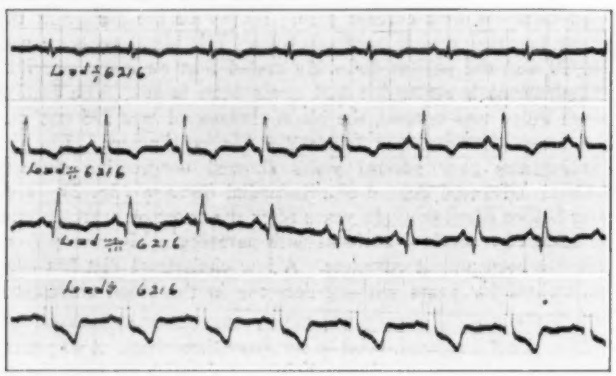

Fig. 2 (case 2).—Tracings showing changes indicative of advanced degree of myocardial damage.

heart in both oblique views revealed no chamber enlargement, which was evidence against any previous, persistent hypertension. The urine was normal; the fasting blood sugar was 129 mg. per hundred cubic centimeters; the blood cholesterol was 333 mg. per hundred cubic centimeters of plasma. The electrocardiogram did not reveal any abnormality. The patient gradually improved on a regimen consisting essentially of modified activity, a low cholesterol diet and xanthine vasodilating drugs.

Significant Features.—Familial history of heart disease; coronary insufficiency in the absence of diabetes or persistent hypertension; hypercholesteremia; onset of cardiac symptoms and xanthoma of the skin at approximately the same time.

CASE 5.—N. B. O., a married woman [2] aged 45, first entered the clinic in March 1941 complaining chiefly of pains in the knees and mild precordial pain following exertion. She stated that, twenty years before, nodules appeared on both achilles tendons and yellow plaques were noticed on both eyelids. Five

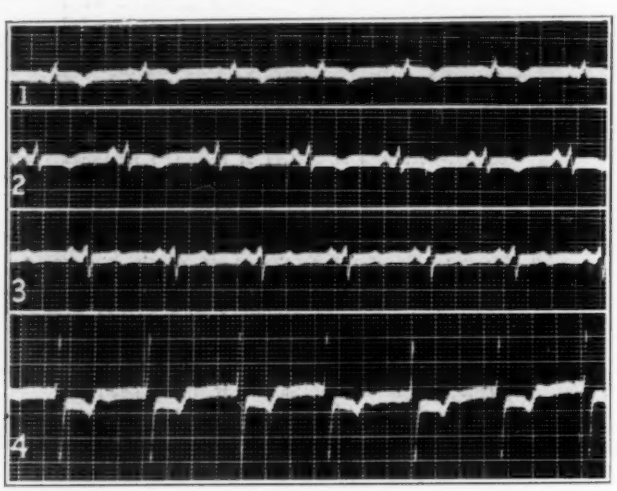

Fig. 3 (case 3).—Tracings made one week after attack of severe chest pain, revealing infarction of the anterior wall.

years after their appearance the tendon nodules were excised because their large size had caused discomfort. They promptly recurred. The family history revealed that two brothers had similar skin lesions and one brother had sustained an acute coronary thrombosis in his early forties. Examination revealed large, subcutaneous masses the size of a fist on each achilles tendon, with smaller nodules along the tendons of the dorsum of the hands and feet. There were yellow nodules at the knees and elbows and yellowish plaques on the upper and lower eyelids. Blood pressure was 130/80; the basal metabolic rate was —15 per cent. The blood cholesterol was 465 mg. per hundred cubic centimeters. The fasting blood sugar level was normal. An electrocardiogram was normal (fig. 4 *A*). Immediately after exercise, however, there was epigastric distress and a depression of the ST segment in leads 1 and 2 and inversion of the T wave in lead 4 F (fig. 4 *B*). After one hour of rest the electrocardiogram was again normal (fig. 4 *C*).

A diet free of animal fat was prescribed but follow-up was incomplete, as she did not return to the clinic and could not be traced.

Significant Features.—Familial history of xanthomatosis and early heart disease; a twenty year interval between the appearance of the skin and tendon lesions and the heart symptoms; normal blood pressure; hypercholesteremia.

CASE 6.—C. N., a married woman aged 31 entered the clinic in 1939 because she had noticed swellings on the achilles tendons. The family history was not significant. Examination was negative except for the hard, nodular swellings on both achilles tendons. The blood pressure was 116/74. Biopsy of the nodules revealed typical evidence of xanthomatosis. The blood cholesterol at this time (August 1939) was 333 mg. per hundred cubic centimeters; the basal metabolic rate was —21 per cent; the urine was normal. The patient was put on a low cholesterol diet, and desiccated thyroid was prescribed but was not well tolerated. In January 1940, one year after

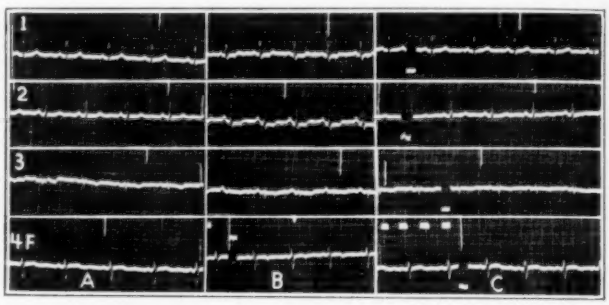

Fig. 4 (case 5).—Tracings made (*A*) at rest, (*B*) with exercise showing depressed ST segment in leads 1 and 2 and inverted T_4, (*C*) after one hour of rest; electrocardiogram is again normal.

the appearance of the tendon lesions, she began to complain of precordial palpitation. Clinically, extrasystoles were noted. In June 1940 she began having precordial pain. An electrocardiogram at this time was not considered definitely significant but an electrocardiogram taken eight months later showed a flattening of T_1 and T_2 and an inversion of T_4 (fig. 5). During this time, despite the low cholesterol diet which she followed, repeated determinations showed a blood cholesterol of between 430 and 450 mg. per hundred cubic centimeters and cholesterol esters ranging between 290 and 320 mg. per hundred cubic centimeters.

Significant Features.—Xanthomatous nodules of tendons; hypercholesteremia; heart symptoms and electrocardiographic changes at the age of 32 in the absence of diabetes or hypertension; no response on low cholesterol diet.

COMMENT

The cases presented are quite typical of the syndrome of xanthomatosis associated with coronary disease and serve to illustrate the significant features of this condition.

1. *Familial Tendency.*—This was present in 4 of our 6 cases. The available evidence in the literature in which xanthomatous families have been traced through four generations reveals that it is a dominant hereditary disease. Müller [1] presented 68 cases occurring in seventeen families. Recently a family was described in

which 4 children between the ages of 6 and 23 years died of xanthomatosis of the cardiovascular system. The authors [3] discussed thoroughly the genetic aspects of the disease and stated that although it might be a dominant factor it could be explained also as simple recessiveness.

2. *Age at Onset of Heart Disease.*—In 2 of our cases (1 and 3) acute coronary thrombosis occurred at the age of 32 and 33 respectively. In 5 the initial evidence of cardiac involvement was relatively early in life. Apparently this is a disease which may affect the cardiovascular system of all age groups. In the literature, involvement of the coronary artery in the first decade of life has been reported. On the other hand the first manifestations may not occur until middle age or later in life.

3. *Sex.*—Our patients were equally distributed between the two sexes, in contradistinction to the usual predominance of coronary disease in males.

4. *Type of Cardiovascular Involvement.*—Coronary insufficiency was present in all cases. In 1 the cerebral vessels were also sclerotic. Though coronary disease is the most frequent type of vascular involvement, the heart valves are occasionally affected and cases have been reported in which the aorta and pulmonary arteries

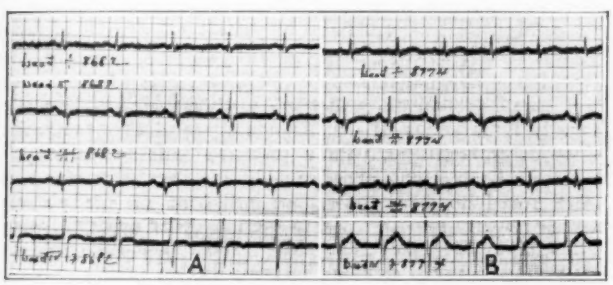

Fig. 5 (case 6).—*A*, June 1940. *B*, eight months later; T_1 and T_2 are now flat; T_4 is inverted.

were greatly narrowed. Peripheral vessels are often sclerotic, and claudication may be the chief or primary symptom.

We have seen 2 cases of tendon sheath xanthomatosis in young adults with hypertension and coronary disease. We have not included them in this series because the coronary sclerosis may be secondary to the hypertension rather than xanthomatous in origin. It is our opinion that in these cases the hypertension is secondary to sclerosis of the renal vessels, an aftermath of the disordered cholesterol metabolism. This interpretation is supported by the fact that the tendon sheath lesion had been present for several years prior to the onset of the hypertension.

5. *Types of Xanthomatosis of the Skin Associated with Cardiovascular Disease.*—Basically two types of cutaneous xanthomatosis exist—xanthoma tuberosum and xanthoma disseminatum. The latter, a more rare disturbance, is characterized by multiple small yellowish papules scattered over the flexural surfaces of the body and the mucous membranes. In this type the blood lipids are within normal limits and diabetes insipidus is not infrequent. This disseminated variety is rarely associated with cardiovascular disease.

3. Bloom, David; Kaufman, S. R., and Stevens, R. A.: Hereditary Xanthomatosis, Arch. Dermat. & Syph. **45**: 1-18 (Jan.) 1942.

Xanthoma tuberosum, the most common variety, is characterized by lesions occurring predominantly on the extensor surfaces of the extremities. They may be single or multiple, small or large firm nodules more often on the elbows, knees or knuckles. The cutaneous

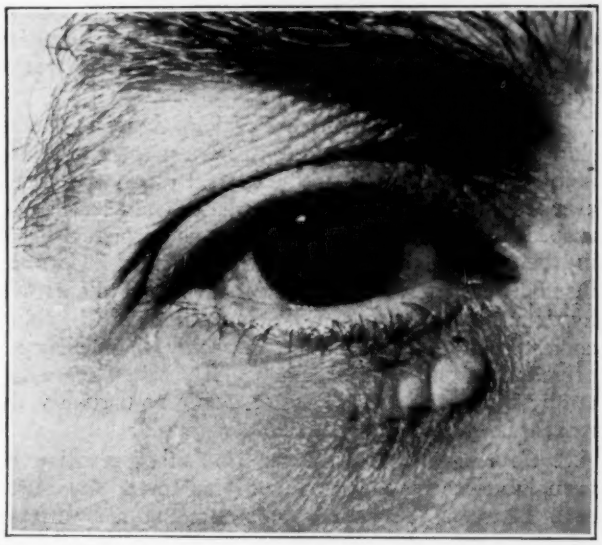

Fig. 6.—Xanthoma of eyelid, showing minimal lesion.

nodules are yellow or chamois colored, and the tendon or tendon sheath xanthomas are subcutaneous without alteration in the color of the overlying skin. In this type there is generally a definite elevation of the blood cholesterol level and an increase in the content of total blood lipids.

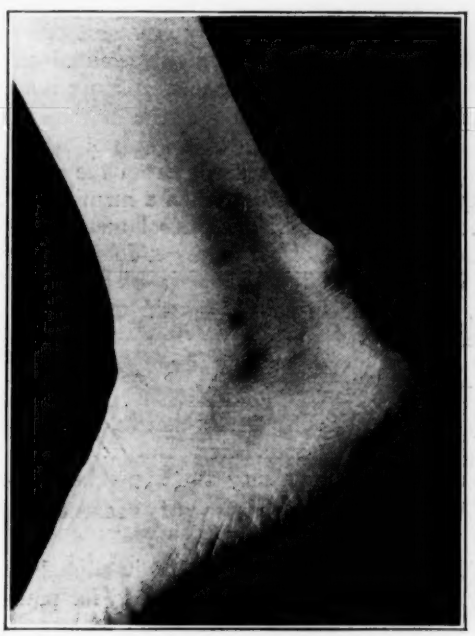

Fig. 7 (case 2).—Xanthoma of achilles tendon.

Xanthoma palpebrarum, often classified as a separate variety, may belong in the tuberous group and is frequently found associated with other nodules or may precede their appearance. Even when present alone, there is frequently a moderate hyperlipemia and cardiovascular xanthomatosis.

6. *Variations in Blood Cholesterol.*—Hypercholesteremia of varying degree was present in all 6 cases. The blood cholesterol is usually elevated in this syndrome, but not necessarily so. The three cardinal signs—hypercholesteremia, skin or tendon xanthoma and coronary insufficiency—frequently occur together, but any one or two of the triad may be absent or precede the other. In 2 of our patients the skin and heart involvement occurred simultaneously, and in 1 there was no skin or tendon sheath xanthomatosis.

7. *Diagnosis in the Absence of Skin Lesions.*—When skin or tendon sheath xanthomas are present, attention is immediately directed to the correct diagnosis. However, there are certain features that should lead one to suspect the presence of xanthomatous coronary disease in the absence of the superficial lesions. Coronary insufficiency in women in the absence of diabetes or hypertension calls for a determination of the blood cholesterol. Likewise when coronary insufficiency is present in young adults, particularly when there is a family history of early cardiac death or coronary disease, this syndrome should be considered.

8. *Course.*—Although our period of observation has been limited, there does not appear to be any difference between the course of xanthomatous coronary sclerosis and arteriosclerotic coronary disease. Acute coronary thrombosis may occur at any time. However, the possibility of modifying or arresting the progress of this type of coronary disease by therapy is more hopeful than in arteriosclerosis.

9. *Therapy and Prophylaxis.*—Therapy is meager. A low cholesterol diet may reduce the hypercholesteremia. This occurred in only 1 of our 3 patients who followed the diet faithfully. Thannhauser [1] has shown that on such a diet the xanthomatous patient with a hypercholesteremia loses a large amount of cholesterol from the body. In the diet only animal sterols are omitted, as plant and vegetable sterols are not absorbed by human beings. Although the administration of thyroid is recommended, we have not observed any beneficial effect from its use. From the standpoint of prophylaxis it appears that when a member of a family manifests a disorder of cholesterol metabolism it may be wise for the rest of the family to follow a low cholesterol diet. When the diagnosis of xanthomatosis is made, the physician should investigate other members of the family.

SUMMARY

1. In the 6 cases of xanthomatosis with coronary artery disease in young adults that have been described there are three characteristic features: skin xanthomatosis, coronary insufficiency and hypercholesteremia.

2. A strong familial tendency is present and the disease often appears early in life.

3. Therapy consists of a diet low in animal cholesterol and other measures usually prescribed for patients with coronary artery disease. The familial occurrence affords an opportunity for the prophylactic institution of a low cholesterol diet in other members of the family as yet unaffected.

4. By recognizing and segregating this type of coronary artery disease we may anticipate a more hopeful therapeutic outlook than in patients with the usual coronary artery disease.

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LEUKEMIA IN PREGNANCY

WITH REPORT OF A CASE

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Leukemia is a rare complication of pregnancy. Forkner,[1] reviewing the literature up to 1938, found 53 cases reported and of these the diagnosis was questionable in 5 instances. Presenting 1 of their own, Grier and Richter [2] in 1939 were able to collect a total of 75 cases, but 13 of these were mentioned only bibliographically. We discovered another reported by Bentivoglio [3] in 1936 which was not included in this series. From 1939 to the present writing there have been 2 additional cases reported in the foreign literature.[4] These, with the 1 described here, bring the present total reported up to 79.

In our case chronic myelogenous leukemia was discovered early in pregnancy and undoubtedly preceded gestation. The disease was also complicated by preeclamptic toxemia. The mother was successfully delivered of a living normal child by cesarean section.

REPORT OF CASE

Mrs. H. M., aged 32, white, was first seen by her physician, Dr. Homer Brayton of Dorchester, Mass., Feb. 24, 1942. Her last period, following a normal menstrual cycle, began on Jan. 1, 1942. Physical examination revealed that the patient was poorly nourished, with a pale and sallow skin, a pulse rate of 84 and blood pressure 110/70. The heart and lungs were found to be normal, but palpation of the abdomen revealed a firm smooth mass, in the left upper quadrant, which extended to the iliac crest. The patient had discovered the mass but associated it with the possibility of pregnancy. She complained of several recent episodes of epistaxis, profuse night sweats and moderate weakness for two to three months preceding her first visit but otherwise had been in excellent health.

Blood examination revealed white blood cells 140,000, red blood cells 1,700,000, hemoglobin 45 per cent (Sahli), polymorphonuclear leukocytes 6 per cent, eosinophilic myelocytes 25 per cent, basophilic myelocytes 5 per cent, myelocytes 40 per cent, metamyelocytes 21 per cent, lymphocytes 3 per cent, blast cells 2 per cent and nucleated red blood cells 2 per cent. The red blood cells showed some achromia and some slight variation in size and shape; the platelets were normal. The Wassermann test was reported negative. A diagnosis of chronic myelogenous leukemia was made at this time. The patient received two small doses of 100 roentgens to the spleen, one on March 12 and a second on April 16. In May a definite diagnosis of pregnancy was established.

The antepartum course progressed normally until the thirty-second week, when signs of preeclamptic toxemia developed. The blood pressure rose to 140/90 and pitting edema of the ankles was noticed. She was placed on a salt free diet and advised to take additional rest, but by mid-September the blood pressure reached 150/90. She was confined to bed on a strict regimen, and two weeks later the pretibial edema had increased and the blood pressure had climbed to 180/110. A heavy trace of albumin was found in the urine. The patient was admitted to the Carney Hospital on September 16. The fundus was three

Read before the Boston Obstetrical Society, Jan. 19, 1943.
From the Obstetrical and Gynecological Service, Carney Hospital, Boston.

1. Forkner, C. E.: Leukemia and Allied Disorders, New York, Macmillan Company, 1938, pp. 145-150.
2. Grier, R. M., and Richter, H. A.: Am. J. Obst. & Gynec. **37**: 412-425 (March) 1939.
3. Bentivoglio, F.: Folia gynaec.-demograph., Genoa **33**: 53, 1936.
4. Tschopp, W.: Folia haemat. **61**: 319-333, 1939. Herrnberger.[5] Vignes.[6] Burchenal.[10] Jarmai.[11]

fingerbreadths below the ensiform process with the vertex riding high. The fetal heart was heard in the left lower quadrant, rate 144. The spleen was palpable 12 cm. below the costal margin in the left midclavicular line, smooth and slightly tender. The white blood count was 76,000. Two small hemorrhages were found in the left ocular fundus. These are commonly found in leukemia. A diagnostic roentgenogram of the

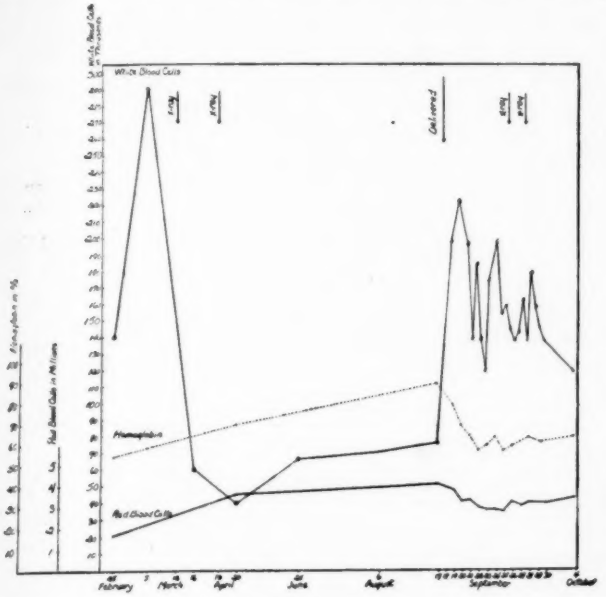

Fig. 1.—Blood studies.

fetus demonstrated no fetal skeletal anomalies. As the preeclamptic toxemia had not responded to conservative measures it seemed advisable to terminate the pregnancy. As the cervix was long and firm, delivery by cesarean section was selected. On September 18, under spinal anesthesia (15 mg. of pontocaine hydrochloride with 1.5 cc. of dextrose) a transverse low cervical cesarean section was performed (R. J. H.) and a normal premature female infant weighing 4 pounds 14 ounces (1,928 Gm.) was delivered. There was no difficulty with hemostasis, and the uterus responded excellently to intravenous ergonovine (0.0002 Gm.) and hypodermic pitocin (1.0 cc.). The immediate postpartum course (first twenty-four hours) was marked by a febrile response to 102.4 F., the pulse rose to 120 and massive drenching sweats occurred. Six hours after operation the patient passed approximately 300 cc. of currant jelly clots vaginally, but otherwise the recovery was uneventful. The changes in the blood are recorded in the accompanying chart (fig. 1). Diethylstilbestrol in doses of 2.0 mg. a day was used for suppression of lactation. It should be noted that the day after delivery the white blood count rose rapidly and the red blood count and hemoglobin fell. The spleen showed a relatively rapid increase in size during the first week post partum. Fifty roentgens over the spleen was administered on the eighth and tenth days and the blood picture improved definitely. The spleen decreased in size. Except for a small sterile collection of hemolyzed blood at the lower angle of the wound, which reabsorbed spontaneously, the incision healed normally. Examination of the placenta revealed an unusual number of immature white blood cells in the maternal lacunae, as shown in the photomicrographs (figs. 2 and 3). The infant's blood count at birth was as follows: 25,000 white blood cells, 5,850,000 red blood cells, 126 per cent hemoglobin (Sahli), 65 per cent polymorphonuclear leukocytes, 15 per cent lymphocytes, 5 per cent eosinophils, 6 per cent myelocytes, 4 per cent band forms and 5 per cent nucleated red blood cells. Five days later the blood count showed 11,000 white blood cells, 5,560,000 red blood cells, hemoglobin 125 per cent (Sahli), 63 per cent polymorphonuclear leukocytes, 3 per cent myelocytes, 2 per cent eosinophils, 30 per cent lymphocytes, 2 per cent monocytes and 2 per cent nucleated red blood cells. These blood findings are within normal limits for a newborn infant in good general condition.

The patient was discharged from the hospital Oct. 4, 1942 on the sixteenth day after delivery. The spleen was palpable 5 cm. below the costal margin in the left midclavicular line. The blood count on discharge is reported in figure 1. The baby left the hospital on the sixteenth day in good condition weighing 5 pounds 5 ounces (2,410 Gm.).

The occurrence of amenorrhea is so common in the presence of leukemia that in this case the fact that conception had taken place was not known until the pregnancy was well advanced. Two small doses of x-ray therapy had the excellent effect of lowering the white blood cell count and elevating the hemoglobin and erythrocytes. Also the spleen was reduced in size so that no further x-ray therapy was deemed necessary after the fourth month of pregnancy.

The patient had a normal antepartum course until the seventh month, when signs of toxemia developed. This is apparently the only case of preeclamptic toxemia complicating leukemia in pregnancy reported thus far. Since the toxemia did not respond to conservative treatment, and induction of labor through the pelvis was not considered feasible, cesarean section was elected.

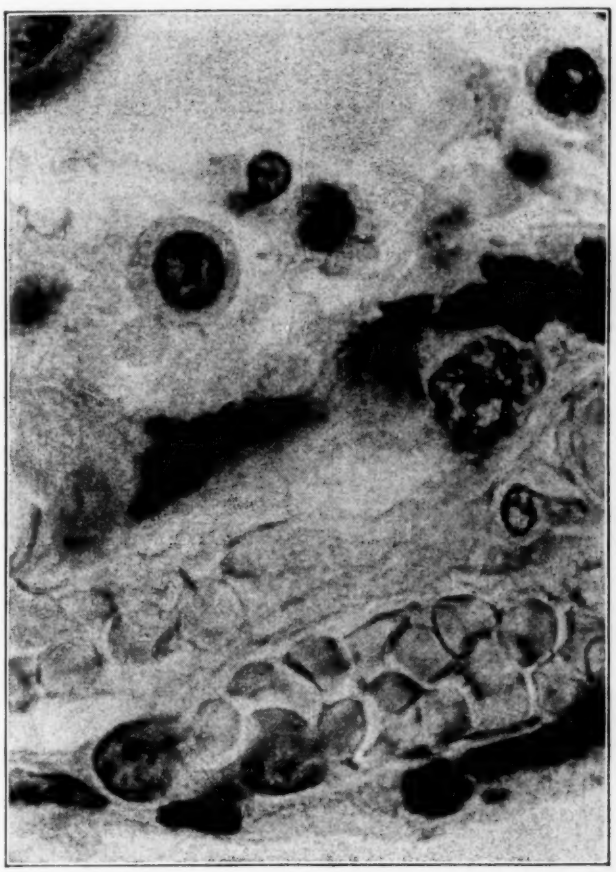

Fig. 2.—Large leukemic cell in the maternal lacuna above the placental villus. Reduced from a photomicrograph with a magnification of 2,100 diameters.

In addition to our case three other leukemic mothers, in the total series of 79 cases, were delivered by cesarean section:

1. Fleischmann [5] in 1923 did a cesarean section at the eighth month on a 30 year old tertipara. Her leukemia developed prior to gestation. The baby was stillborn and the mother died on the eleventh day post partum.

5. Fleischmann, C.: Zentralbl. f. Gynäk. **47**: 1277, 1923.

2. Thamer [6] in 1925 sectioned a 28 year old secundipara in the eighth month. Her leukemia antedated pregnancy by five months. The infant was stillborn and the mother died eleven days post partum.

3. Hüssy [7] in 1934 delivered abdominally a 35 year old tertipara who developed leukemia during pregnancy. The section was done at seven and one-half months and, although the infant survived, the mother died twenty-four hours after delivery.

The case described by us would seem, therefore, to be the first thus far reported in which a pregnancy complicated by leukemia was successfully terminated by cesarean section. In keeping with the experience of other authors, hemostasis was easily obtained during the operative procedure and postpartum hemorrhage did not occur.

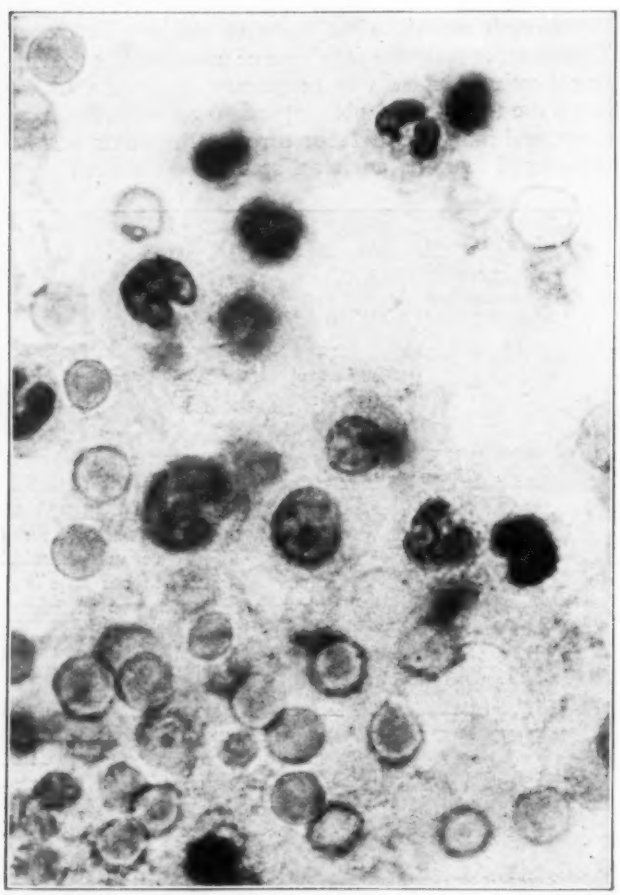

Fig. 3.—Several large leukemic cells. The tip of a placental villus in the right lower corner. Reduced from a photomicrograph with a magnification of 2,100 diameters.

Contrary to the statement of Herrnberger,[8] a rise rather than a fall in white blood count occurs immediately after delivery. Not only is this borne out in this case, but in Herrnberger's own reported case there occurred a sharp rise in the white blood cell count immediately following the termination of pregnancy. Chronic lymphatic leukemia has been reported only once in pregnancy. As Vignes [9] pointed out, this probably is due to the tendency of the lymphatic cells to infiltrate the adnexa, precluding the possibility of conception. On the other hand, acute lymphogenous leukemia has been reported not infrequently.

6. Thamer, H.: Marburg, 1925.
7. Hüssy, P.: Schweiz. med. Wchnschr. **64**: 629, 1934.
8. Herrnberger, K.: Zentralbl. f. Gynäk. **63**: 2309-2317, 1939.
9. Vignes, H.: Presse méd. **47**: 1460-1461, 1939.

COMMENT

The progress of this case substantiates the opinions of Grier and Richter [2] that a patient who becomes pregnant early in the course of chronic myelogenous leukemia will usually give birth to a living infant and that in 4 out of 5 instances she will survive the delivery. Forkner [1] also believes that pregnancy does not accelerate the course of chronic leukemia. In our case the leukemic process tended to regress during pregnancy.

The occurrence of leukemia in pregnancy tends to shed some light on the etiology of the morbid process. It is significant that a leukemic mother has never given birth to an infant with leukemia. It has been postulated that a chemical or hormonal factor may be responsible for leukemic stimulation of the hemopoietic tissue. However, it is evident that either such a substance does not exist or it is incapable of passing the placental barrier. Moreover, in experimental studies Burchenal [10] has found it impossible to transmit leukemia of mice to the fetus by inoculation of the mother. Jarmai [11] found it possible to inoculate chick embryos with a transmissible virus of chicken leukemia. This suggests that, fundamentally, the development of leukemia must be dependent on a specific tissue susceptibility.

TREATMENT

It is our impression that pregnancy has apparently no effect on the progress of leukemia. The natural history of this disease is such that the outcome is relatively uninfluenced by treatment although the patient may be symptomatically improved. At present there is no effective treatment for the individual with acute leukemia, pregnant or otherwise. Since leukemia in pregnancy is such a rare disorder, no one has had sufficient personal experience to outline specifically the management of this complication of pregnancy. It seems obvious, however, that sterilization of the leukemic woman or interruption of pregnancy is not advisable. The palliative use of x-ray therapy for chronic myelogenous leukemia in pregnancy should not be withheld. It is possible to irradiate the long bones, the thorax and with due care even the spleen with no deleterious effect to the fetus in utero. The intravenous or oral use of radioactive phosphorus would seem contraindicated because of the direct action on the uterus and its contents. Solution of potassium arsenite, although its value is questioned by some clinicians, can be used without endangering the fetus. Whole blood transfusions are indicated when anemia and thrombocytopenia with attending hemorrhagic tendencies manifest themselves. In the management of the pregnancy the presence of strictly obstetric complications such as cephalopelvic disproportion, toxemia and placenta previa can be controlled on their obstetric indications. In the case reported the preeclamptic toxemia was treated as it would have been without the presence of leukemia.

SUMMARY AND CONCLUSIONS

1. Leukemia complicating pregnancy is a rare entity; a total of 79 cases have been reported.

2. The natural course of leukemia is apparently uninfluenced by gestation. Leukemia per se is therefore not an indication for the interruption of pregnancy.

3. Chronic leukemia in pregnancy is a problem which can be intelligently handled in the majority of cases only by the combined efforts of the hematologist and the obstetrician.

1101 Beacon Street.

10. Burchenal, J. H.: Am. J. Cancer **39**: 309-314 (July) 1940.
11. Jarmai, K.: Deutsche tierarzt. Wchnschr. **41**: 418, 1933.

POSTOPERATIVE, FOCAL, NONSEPTIC NECROSIS OF VERTEBRAL AND CEREBELLAR ARTERIES

WITH RUPTURE AND SUBARACHNOID HEMORRHAGE

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Subarachnoid hemorrhage caused by focal, nonseptic necrosis of the vertebral artery or of its branch, the posterior inferior cerebellar artery, is an unusual occurrence. We here record our observations made on 4 elderly, generally slightly hypertensive patients who showed no evidence of endocarditis or of a general or local infectious process, who died of this condition within a few days of uncomplicated abdominal operations. Only the apparently relevant features of the histories and examinations are given.

There is a voluminous literature on the subject of subarachnoid hemorrhage; however, much of this is in reference to ruptured congenital aneurysms. Sands,[1] in a recent study of subarachnoid hemorrhage, reported 120 cases and pointed out that it "is caused by (1) trauma, (2) arteriosclerotic degeneration of vessel walls, (3) septic or infectious emboli, (4) ruptured intracranial aneurysms, (5) massive cerebral hemorrhage invading the subarachnoid space, (6) intraventricular hemorrhage, (7) blood dyscrasias and (8) ruptured vascular neoplasm." In addition to the foregoing there is a relatively large group which Sands listed as of "unknown or undetermined cause."

Necrosis of the arteries of the brain is a well known phenomenon in large infarcts and we have also seen extensive necrosis of meningeal blood vessels in many cases of tuberculous meningitis or septic meningitis as well as in cases of "periarteritis nodosa," septic endocarditis and other conditions, but we have not seen any of these that had vessels ruptured and produced extensive subarachnoid hemorrhage. As a rule in such cases the entire wall of a small artery becomes necrotic and not a small segment of the circumference, leaving the remaining portion of the wall normal. Winternitz and LeCompte [2] produced varying degrees of inflammation and proliferation of the walls of arteries by injecting organisms of different degrees of virulence into the walls of arteries but did not produce areas of focal necrosis. We have been unable to find any record in the available literature of a case of subarachnoid hemorrhage due to rupture of a noninflammatory necrotic focus in the wall of a cerebral artery.

REPORT OF CASES

CASE 1.—An educator aged 62 was registered at the Mayo Clinic on Feb. 2, 1942 for a general examination and consideration of a right inguinal hernia. Examination disclosed a systolic blood pressure of 160 mm. of mercury and a diastolic pressure of 100 mm. There were slight hypertensive sclerosis of the retinal arterioles and slight sclerosis of the choroidal vessels. An apparently old retinal detachment was noted in the lower temporal sector on the right. Bilateral direct inguinal hernias were present. Numerous leukocytes were noted in the prostatic secretion. An occasional erythrocyte was found in the urine. Cystoscopic examination gave negative results.

On February 24, with the patient under spinal anesthesia, both inguinal hernias were repaired. On February 28 he complained of an occipital headache, vomited, became confused, had a convulsion and died.

At necropsy the recent operative incision had the usual appearance of a wound four days old. The heart was hypertrophied and weighed 505 Gm., in contrast to an estimated normal weight of 370 Gm. The arteriosclerosis of the aorta was estimated as grade 1 + (on a basis of 1 to 4, in which 1 designates the least and 4 the greatest degree of arteriosclerosis) and the other large systemic arteries were graded similarly. The prostate was slightly enlarged, but there were no other findings of any significance aside from those of the central nervous system.

There was extensive subarachnoid hemorrhage. We estimated the extravasated blood at about 200 cc.; it had completely filled the subarachnoid space and some had extended into the ventricles. After removing much of the blood we found that there was arteriosclerosis of the cerebral vessels graded 2 +, that there was no aneurysm of the vessels arising from the carotid arteries and that the circle of Willis did not show any abnormalities. There were symmetrical fusiform dilatations of the vertebral arteries about 0.5 cm. above their entrance into the cranial cavity; these dilatations were each 1 cm. long. The vertebral arteries had become normal about 3 cm. before fusing to form the basilar artery. After removing more blood we found a small hole about 1 mm. in diameter in the left posterior inferior cerebellar artery 1.5 cm. from its origin at the left vertebral artery (fig. 1). There was no branch of the artery at the site of perforation, and the artery seemed normal proximal and distal to the defect (there was no dilatation or aneurysm). The other arteries in the posterior fossa were normal.

Fig. 1.—Basilar, vertebral and posterior inferior cerebellar arteries. The arrow indicates the point of rupture in the left posterior inferior cerebellar artery. The defect was in the anterior aspect of the vessel wall.

Microscopic sections were prepared from many of the cerebral and cerebellar vessels as well as from many vessels of other organs. These sections were stained with hematoxylin and eosin, van Gieson, Weigert elastin and elastin H stains as well as Giemsa, Brown Gram, mucicarmine and cresyl violet. Except for some arteriosclerotic changes of a minor degree, all vessels were normal. However, sections of the left posterior

From the Section on Pathologic Anatomy (Dr. Kernohan) and the Section on Neurology (Dr. Woltman), Mayo Clinic.

1. Sands, I. J.: Diagnosis and Management of Subarachnoid Hemorrhage, Arch. Neurol. & Psychiat. **46**: 973-1005 (Dec.) 1941.

2. Winternitz, M. C., and LeCompte, P. M.: Experimental Infectious Angiitis, Am. J. Path. **16**: 1-12 (Jan.) 1940.

inferior cerebellar artery at the site of the rupture showed a small region of complete necrosis of the vessel wall. This region of necrosis included only a quarter of its circumference. The necrotic focus was wider at the adventitia than in the media, while the internal elastic lamina had curved outward, lining the inner third of the side of the defect (fig. 2). There was no inflammatory reaction in the media or intima (fig. 3),

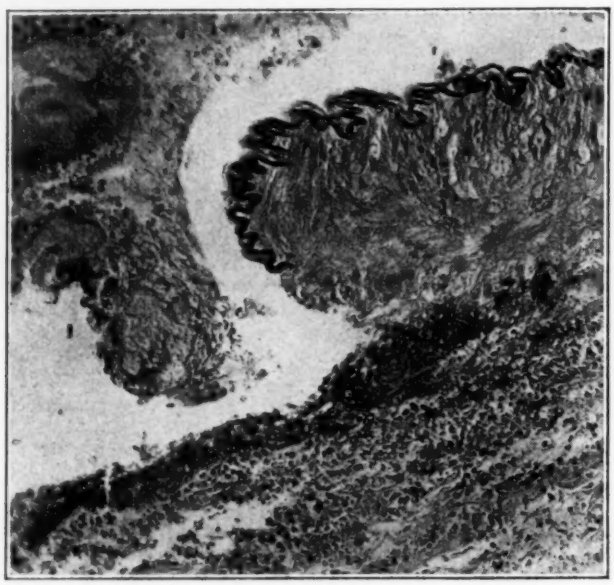

Fig. 2.—The edge of the defect in the arterial wall showing the inflammatory reaction in the adventitia and the absence of inflammation in the media and intima (elastin H stain; × 160).

but where the necrosis had involved the adventitia beyond the defect in the wall were many polymorphonuclear leukocytes. In figures 2 and 3 can be seen the extent of necrosis along the adventitia of the vessel. There was no evidence of any inflammatory or infectious material in the lumen, intima or media of the artery. Bacteriologic stains did not show any organisms anywhere in or around the wall or in the necrotic portion of the adventitia of this blood vessel.

CASE 2.—A housewife aged 62 was registered on May 22, 1941 as a patient at the Mayo Clinic with the complaint of epigastric distress of several years' duration. Roentgenograms disclosed a duodenal ulcer. The blood pressure was 172 mm. of mercury systolic and 110 mm. diastolic. The retinal arterioles were slightly narrowed and sclerotic, chronic hypertensive type, and the choroidal vessels were slightly sclerosed. Urea in the blood was reported as 32 mg. per hundred cubic centimeters.

On May 30, 1941, with the patient under inhalation anesthesia with ethylene, oxygen, carbon dioxide and ether, posterior gastroenterostomy was performed because of two subacute ulcers on the posterior wall of the duodenum.

Two days after operation the patient complained of pain in her head and became stuporous. The pupils were pinpoint, the neck was not rigid and Babinski's sign was positive on the left. The patient died thirty minutes after the onset of the headache.

At necropsy the recent operative site showed signs of healing, and there was a chronic duodenal ulcer with evidences of many healed ulcers (scars) and partial obstruction of the lumen of the duodenum. There was some pancreatitis but no fat necrosis. The remainder of the general examination gave essentially negative results except for hypertrophy of the heart, which weighed 365 Gm. in contrast to an estimated normal of 275 Gm. There was arteriosclerosis of the aorta and larger arteries graded 2 on a basis of 1 to 4.

Examination of the brain revealed the subarachnoid space to be filled with blood and blood clots. The arteriosclerosis of the main arteries at the base of the brain was graded 1 on a basis of 1 to 4. There were no anomalies or aneurysms of the circle of Willis or of the basilar or vertebral arteries. In searching for a source of the subarachnoid hemorrhage a hole 1.5 mm. in diameter was found in the left posterior inferior cerebellar artery less than 1 cm. from its origin from the left vertebral artery.

The results of microscopic examination of the rupture in the artery were identical with those in the previous case. The necrosis extended beyond the defect in the adventitia, the media was free from inflammation or edema and the elastic tissue of the intima followed the defects outward partly across the media. There was no inflammatory reaction anywhere, except some polymorphonuclear leukocytes in the necrotic tissue of the adventitia. No organisms were found after the use of the Brown Gram stain. The other arteries of the brain were normal. Examination of many sections of the pancreas did not show any necrosis of the pancreatic arteries as a possible explanation of the interstitial pancreatitis, which was both acute and chronic.

CASE 3.—A fruit pedler aged 54 came to the Mayo Clinic on June 25, 1941 because of bilateral inguinal and umbilical hernias. The left inguinal hernia had been operated on three times previously. The patient had recovered from rhinitis a few weeks previously. In addition to the hernias, examination disclosed a systolic blood pressure of 176 mm. of mercury and a diastolic pressure of 108 mm. There were minimal narrowing and sclerosis of the retinal arterioles. The tonsils were regarded as a possible focus. The left testicle was atrophied. The leukocytes numbered 15,000 per cubic millimeter of blood. There was a trace of albumin in the urine.

On July 1, with the patient under spinal anesthesia, the left testicle was removed and a hernial opening the size of the hand was closed. Herniorrhaphy was also performed for recurrent umbilical and epigastric hernias.

On the day following the operation, the patient suddenly gasped for breath and died.

The general examination did not reveal anything of significance; the operative wounds were such as one would expect one day after operation. The heart was slightly hypertrophied, weighing 348 Gm. in contrast to an estimated normal of

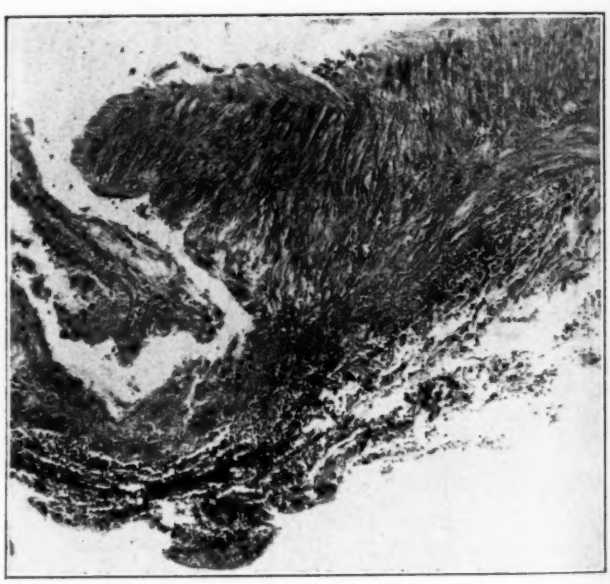

Fig. 3.—The inflammatory reaction to the necrosis in the adventitia. Note the necrosis extending into the adventitia beyond the edge of the hole. Also note the absence of other inflammatory reaction (hematoxylin and eosin stain; × 85).

300 Gm. There was also arteriosclerosis of the aorta, coronary and other arteries, graded 2 on a basis of 1 to 4.

Examination of the brain showed a massive subarachnoid hemorrhage which had extended into the ventricles. The circle of Willis and the vessels derived from it were normal except for arteriosclerosis graded 1. There were small symmetrical dilatations of both vertebral arteries 1.5 cm. proximal to their

union to form the basilar artery. There was a small hole about 1 mm. in diameter at the lower margin of the small dilatation of the left vertebral artery. Microscopic examination of the right vertebral artery showed that it was normal; even the dilatation represented a slight thinning of the wall, but it was not on the basis of arteriosclerosis. The defect in the left vertebral artery was identical with the defects described

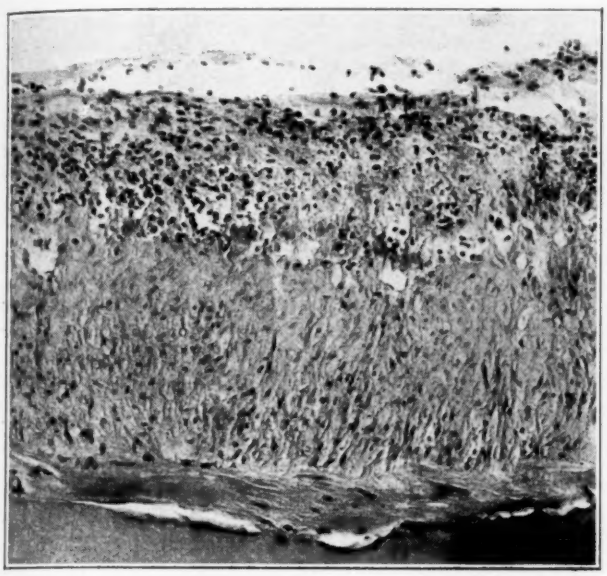

Fig. 4.—A small necrotic focus in the wall of the artery involving the adventitia and outer fourth of the media. No vasa vasorum are present and there is no inflammation in the inner three fourths of the media or the intima (hematoxylin and eosin stain; × 160).

in the posterior inferior cerebellar arteries in cases 1 and 2. In addition, several millimeters below and opposite the defect we found a region of necrosis which included the adventitia and the outer quarter of the media. The inner three fourths of the media and the intima beneath this small region of necrosis were normal. This necrotic focus was partly infiltrated with polymorphonuclear leukocytes (fig. 4). There was no inflammation or thrombus in or beneath the intima opposite this focus. This was the only lesion which we found on any blood vessel—cerebral or systemic, and the posterior inferior cerebellar arteries were normal. We were unable to identify the vasa vasorum in this region of acute degeneration, although in the adventitia of the vertebral artery around it we identified the vasa vasorum as normal. Examination by means of the Brown Gram stains failed to reveal any organisms.

CASE 4.—A truck driver aged 55 was registered first on Aug. 13, 1928 because of attacks of abdominal pain which had been present for a year and a half and which were suggestive of cholecystitis. The blood pressure was 130 mm. systolic and 80 mm. diastolic. Analysis of gastric contents showed a value for total acids of 18 and for free hydrochloric acid of 0. A diagnosis was made of cholecystitis probably associated with stones. On August 20 exploration revealed chronic catarrhal cholecystitis with cholelithiasis, and cholecystectomy and appendectomy were performed.

The patient returned on March 21, 1932 because of flatulence. Fractional analysis of gastric contents after a test meal showed a value for total acids of 4 and for free hydrochloric acid of 0. Roentgenograms of the stomach were negative. The systolic blood pressure was 120 mm. of mercury and the diastolic pressure 80 mm.

The patient was registered the third time on June 1, 1942. He reported that he had been quite well until a year previously, but that since then he had had occasional pain in the right hypochondriac region similar to the pains he had experienced before the operation, and that he was troubled with gas and constipation and had lost 30 pounds (13.6 Kg.). The systolic blood pressure was 132 mm. of mercury and the diastolic pressure 80. Fractional analysis after a test meal showed a value for total acids of 8 and for free hydrochloric acid of 0. Roentgenograms of the stomach showed a carcinoma of the pyloric half of the stomach.

On June 4, with the patient under nitrous oxide, carbon dioxide, oxygen and ether anesthesia, exploration was performed and carcinoma of the stomach with perforation into the transverse mesocolon was found. Partial gastrectomy, of the anterior Balfour Polya type, with enteroanastomosis, partial duodenectomy and exteriorization of a devitalized segment of the transverse colon was done. Microscopic studies of the posterior wall of the lesser curvature disclosed a grade 4 flat ulcerating carcinoma 8 cm. in diameter by 1 cm. in depth with extension into the serosa and beginning infiltration of the mesentery and involvement of one lymph node.

Following the operation the patient spoke of having a mild headache. On June 7 at 5:20 p. m., while talking to his wife, he suddenly lost consciousness, and the eyes turned upward and toward the right. Within ten minutes it was observed that the left arm and leg remained motionless. The neck was somewhat rigid and both plantar responses were slightly extensor. The systolic blood pressure was 210 mm. of mercury and the diastolic pressure 100. Two hours later the patient was more responsive. The temperature had risen to 105 F. On June 8 and 9 he improved considerably and his headache was less severe, but he remained somewhat confused. On June 10 at 2:40 p. m. the patient again complained of severe pain in his head, lost consciousness and at 3 p. m. died.

Necropsy showed healing of the operative wounds and there was no residual carcinoma or evidence of inflammation. The heart was hypertrophied and weighed 383 Gm. in contrast to an estimated normal of 300 Gm. There was arteriosclerosis of the aorta graded 1 and of the coronary arteries graded 2, on a basis of 1 to 4. There were no other findings of any significance in the general necropsy.

Fig. 5.—The edge of a necrotic but nonruptured focus. Except for the fact that it has not ruptured, it is similar to the lesions in the foregoing cases (hematoxylin and eosin; × 105).

Examination of the brain revealed a massive subarachnoid hemorrhage, but none was present in the ventricles. There was arteriosclerosis of the larger cerebral arteries graded 1 on a basis of 1 to 4. There were no aneurysms or anomalies of the blood vessels composing or derived from the circle of Willis. There was a small hole about 1.5 mm. in diameter in the right vertebral artery, 5 mm. above the origin of the

right posterior inferior cerebellar artery; this ruptured vessel was evidently the source of the subarachnoid hemorrhage. There was no hemorrhage in the substance of the brain in this case or in any of the preceding ones. The other arteries of the posterior fossa were normal.

Microscopic examination of many of the cerebral arteries showed that all were normal except the right vertebral artery. Sections through the site of rupture revealed the fact that it was identical with the defects in the ruptured arteries of the other three cases: namely, necrosis with localized inflammatory reaction of the adventitia, a truncated defect in the media with no evidence of necrosis at the edge of the hole and the internal elastic lamina curving outward, through the inner half of the defect. As in previous cases there was no inflammation in media or intima even at the edge of the rupture. In the arterial wall opposite the rupture was a truncated region of necrosis with the broader base at the adventitia and the narrower apex at the intima (fig. 5). The internal elastic lamina was not ruptured but was swollen and appeared to be undergoing early necrosis or degeneration (fig. 6). There were a few polymorphonuclear leukocytes present between the elastica and the endothelium of the intima. The endothelium was intact beneath this focus of necrosis except at one place, where it had disappeared, and blood was escaping from the lumen of the

Fig. 6.—The swollen degenerating intimal elastic lamina opposite the focus of necrosis in the arterial wall (elastin H; × 105).

artery into the wall of the vessel and was burrowing between the outer portion of the media and the adventitia, which was almost completely necrotic. This blood between the media and the adventitia had the appearance of an early dissecting aneurysm. The endothelium of the intima was otherwise intact and so there was no mural thrombus.

There were several smaller foci of necrosis which varied much in size and depth; some included only the adventitia and others extended varying depths into the media, but there was only one focus which extended to the intima. These smaller foci, if deep, were wedge shaped but, if superficial, were elliptic with their base in the adventitia, and the concave portion extended deepest into the media. Most of these foci were quite recent, since there was no cell reaction in the media. In most foci the only reaction was in the adventitia, and there it was represented by some polymorphonuclear leukocytes; there were no lymphocytes in or around these small necrotic regions. In two places erythrocytes had replaced the media of the arterial wall, only the intima and the adventitia remaining intact, but there was no necrosis or cell reaction at these intramural hemorrhages, which simulated early dissecting aneurysms. The source of the blood could not be found and the intima was intact. Bacteriologic stains failed to reveal any organisms in any of these foci of necrosis.

There was no obvious explanation of the foci of necrosis and the small intramural hemorrhages. The vasa vasorum were normal in the adventitia of the artery except at the foci of necrosis, where we could not see any vasa vasorum. They were obliterated, but whether this obliteration was the cause or the result of the necrosis was impossible to determine—the necrosis had destroyed the evidence. It was possible that the regions of necrosis were small infarcts, the result of an occlusion of the vasa vasorum. It was also possible that the initial lesion was a small intramural hemorrhage followed by necrosis of the wall, or a third possibility was necrosis as the result of occluded vasa vasorum followed by hemorrhages. Either one alone, or the combination of two, could have been responsible, and since there was no blood pigment in any necrotic region we think that hemorrhage was not the primary factor. Arteriosclerosis was present only to a minor degree in this as in the other 3 cases, so we think that the necrosis was not on the basis of arteriosclerosis.

COMMENT

We were at a loss to find some common denominator to explain the focal necrosis in the walls of a cerebellar artery as the source of the subarachnoid hemorrhage in the foregoing 4 cases. In all 4 cases there was some evidence of elevation of blood pressure with slight cardiac hypertrophy and, in all, uncomplicated surgical operations had been performed. These are common findings and the foregoing complication is rare. There was no other finding common to all 4 cases. We have been unable to find a previously reported case, but it is possible that similar cases have been included in the past in the group of cases of spontaneous subarachnoid hemorrhage designated by Sands as of "unknown or undetermined cause." It seemed strange to us that we should encounter four such postoperative complications in one year. We examined anew our previously collected cases of unexplained subarachnoid hemorrhage but failed to find any lesion or rupture of any vertebral or posterior inferior cerebellar artery. The cause of the necrosis is undetermined and we have been unable to relate it to the surgical procedures, anesthetic or medication before or after operation.

General arteriosclerosis was not advanced in any of the cases in spite of the age and evidence of hypertension in all 4 patients, while the arteriosclerosis of the cerebral arteries was even less severe than of the systemic arteries. The arteriosclerosis was minimal in the vertebral and posterior inferior cerebellar arteries, and this was confirmed by microscopic examination. There was no evidence of a mycotic aneurysm at the sites of the ruptures; moreover, there was no source from which an infected embolus could arise and the ruptures were not at the origin of a branch in any of the arteries. There was no elevation of temperature before or after the operations. Bacteriologic studies of histologic preparations of the lesions gave negative results. There was no evidence of an infectious process in the organs in general, except in the second case, in which there was interstitial pancreatitis; however, there was no hemorrhage into the pancreas and we were unable to find acute degenerative changes in its blood vessels. The lesions in the walls of the arteries in these cases did not simulate the changes seen in periarteritis nodosa, since the necrosis seemed to start in the adventitia rather than in the media, they were limited to one artery in each case and there was little periarterial inflammation and no intimal reaction. The points of rupture were unlike those of an atheromatous plaque; there was acute degeneration and not a chronic degenerative process such as is seen in atheromatous lesions. In 1 case there

were slight bulgings of the vertebral arteries, but these were not the result of atheromatous weakening of the wall of the arteries, and such bulging of the vertebral arteries is seen fairly commonly at necropsy of elderly patients.

Little information could be obtained as to the nature of the process in the first 2 cases, but in case 3 and particularly in case 4 we found in the wall adjacent to the rupture early and unruptured foci of necrosis. These foci seemed to have their origin in the adventitia of the artery and in some the necrosis had extended into the media, while in one rather large focus of necrosis it extended down to the intima and even the internal elastic lamina showed evidence of early degeneration. This was a truncated region of necrosis with the base in the adventitia. These smaller foci of necrosis —shallow and deep—suggested to us regions of infarction. In recent years there have been some excellent studies of the blood vessels of the central nervous system and changes with age by Baker,[3] Cobb and Blain,[4] Hackel,[5] Thoma,[6] Ranke [7] and others, but there was no mention of necrosis or of the blood supply of the walls of these vessels. Even Winternitz, Thomas and LeCompte [8] did not describe vasa vasorum in the cerebral arteries. Our own studies showed us that vasa vasorum are normally present in the walls of vertebral arteries, but what would be the result of occlusion of one or more of these is simply conjecture. It is possible that an infarct of the wall of the artery would follow, and the foregoing lesions simulate infarcts. We do not have any direct evidence that there was an occlusion of any of these vasa vasorum prior to the degeneration of the wall, but these small vessels were not patent in the regions of necrosis at the time of our examination. Occlusion of the vasa vasorum of any vessel is probably a rare occurrence; however, it is possible for this to occur as the result of rapid lowering of blood pressure.

SUMMARY

In 4 cases focal necrosis occurred in either the posterior inferior cerebellar arteries (2 cases) or in one vertebral artery (right, 1 case; left, 1 case), following comparatively simple uncomplicated abdominal operations. The foci of necrosis had ruptured and led to massive subarachnoid hemorrhage. We have been unable to find records of similar cases in the available literature but suggest that in some cases subarachnoid hemorrhage of undetermined origin might possibly have had its origin in a manner similar to that of the foregoing cases. We have considered various possible causes for the foci of necrosis starting in the walls of these vertebral vessels and have suggested that they might represent focal infarcts of the walls of the arteries. Some future work on the blood supply of the walls of the vertebral arteries and the vasa vasorum of these vessels remains to be done before an answer to such a hypothesis is obtained.

3. Baker, A. B.: Structure of the Small Cerebral Arteries and Their Changes with Age, Am. J. Path. **13:** 453-462 (May) 1937.
4. Cobb, Stanley, and Blain, Daniel: Arteriosclerosis of the Brain and Spinal Cord, in Cowdry, E. V.: Arteriosclerosis, New York, Macmillan Company, 1933, chapter 14, pp. 397-429.
5. Hackel, W. M.: Ueber den Bau und die Altersveränderungen der Gehirnarterien, Virchows Arch. f. path. Anat. **266:** 630-639, 1928.
6. Thoma, R.: Ueber die Genese und die Lokalisationen der Arteriosklerose, Virchows Arch. f. path. Anat. **245:** 78-122, 1923.
7. Ranke, O.: Zur Histologie und Histopathologie der Blutgefässwand, speziell das Zentralnervensystems (auf Grund neuerer Kenntnisse und Anschauungen über das Mesenchymalnetz und seine Differenzierungsprodukte), Ztschr. f. d. ges. Neurol. u. Psychiat. **27:** 221-245, 1915.
8. Winternitz, M. C.; Thomas, R. N., and LeCompte, P. M.: The Biology of Arteriosclerosis, Springfield, Illinois, Charles C Thomas, 1938.

THE TREATMENT OF PNEUMOCOCCIC PYARTHROSIS

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Our purpose in writing this paper is to present in summary the records of an unusual number of patients with pneumococcic pyarthrosis treated conservatively rather than by conventional surgical methods. The patients, 11 in number, were all seen in the Cincinnati General Hospital and studied in the pneumonia laboratory of the department of medicine.

INCIDENCE

Purulent arthritis is generally regarded as "a rare and grave complication of pneumonia." [1] It was found by Fabyan [2] in 1910 once among 195 cases of lobar pneumonia at autopsy. Bulkley [3] in 1914 collected from the foreign and American literature records of incidence of about 0.1 per cent in pneumonia. Cecil [4] at Bellevue Hospital recorded from 1926 to 1932 an incidence of 0.6 per cent among typed pneumonia cases. Schiff [5] reported from the Cincinnati General Hospital an incidence of 0.5 per cent in the years 1924 to 1929 among 629 cases.

Our present series from 1935 to 1942 inclusive shows an incidence of 0.4 per cent, or 9 cases among 2,322 of typed pneumonia in adults.

Pneumococcic pyarthrosis may occur independent of pneumonia, especially among children. Two such cases are reported here by courtesy of the department of pediatrics, but the bacteriologic study was done in the pneumonia laboratory of the department of medicine.

One must relate pyarthrosis of pneumonia to the bacteremic state; therefore any hospital service receiving late cases or cases of unusual illness will find an increased incidence of septic complications. We are unable to relate the rather high incidence to any other factor, especially specific treatment or exceptional accuracy of diagnosis.

This report is written mainly to record the effects of specific treatment in this "grave" complication of pneumonia.

DIAGNOSIS

In every case of the 11 here reported the pneumococcus was recovered from the blood or from the joint. In 7 instances the organism was recovered from the blood and the joint simultaneously. In 2 instances (cases 7 and 9) we discovered pyarthrosis by aspirating the affected joint of a patient ill with lobar pneumonia and pneumococcemia, but cultures of material taken from the joints were negative. We think that this circumstance, i. e. negative cultures, is not against our diagnosis because drug treatment was well under way when joint cultures were made, and in 1 instance para-aminobenzoic acid was not used in the culture mediums.

This work was aided by a grant from the Lederle Laboratories, Inc.
From the Department of Internal Medicine of the University of Cincinnati and the Cincinnati General Hospital.

1. Heffron, Roderick: Pneumonia, with Special Reference to Pneumococcus Lobar Pneumonia, Commonwealth Fund, 1939, p. 598.
2. Fabyan, M.: Pathological Analysis of 195 Cases of Lobar Pneumonia, Johns Hopkins Hosp. Rep. **15:** 81, 1910.
3. Bulkley, K.: Pneumococcic Arthritis, Ann. Surg. **59:** 71 (Jan.) 1914.
4. Cited by Heffron.[1]
5. Schiff, Leon: Pneumonia in the Adult, Cincinnati J. Med. **11:** 292 (Aug.) 1930.

The diagnosis was usually made at once by finding all the signs and symptoms of acute painful involvement of one or two large joints. In 1 instance (case 10) pneumonia was not even suspected, while in another (case 8) pneumonia was suspected but not proved. When pneumonia is not apparent, the disease must be differentiated from gonorrheal arthritis, to which it is very similar. The differentiation should be made easily if cultures are well managed before the sulfonamides are given. In the main, the pneumococcus is usually grown without much difficulty and the identification made easy by the technic of "typing." Migrating polyarthritis such as that of rheumatic fever was not seen in our experience, nor have we found it described with laboratory proof. Pneumonia due to pneumococci is not rare as a complication of rheumatic polyarthritis. The polyarthritis of serum sickness is well known and easily differentiated from pneumococcic pyarthrosis; it generally resembles rheumatic fever. X-ray studies in our series were of value mainly to exclude osteomyelitis or periostitis. The cases reported here were all so examined and nothing was shown other than slight demineralization of bone and swelling of soft parts. Destruction of cartilage did not occur or else was not shown by x-ray examination or by the functional results at discharge.

In 8 instances there was a single joint involved and in 3 there were two, but there were never more than two. The knee and ankle were most commonly involved. The disease as described in this short series is not different in any way from the usual textbook description except that it has been treated with specifics and therefore has become mild and of short duration. In case 1 pericarditis accompanied pyarthrosis, and meningitis also in case 2. No other suppurating lesion was noted as coincidental. Pneumococcic endocarditis has been found at the Cincinnati General Hospital at autopsy in 39 cases from 1935 to 1942 among typed cases of pneumonia, but only once was there associated pyarthrosis.

TREATMENT

Our treatment has been altogether conservative in that we have relied on specific drugs or serum or the two together with repeated aspirations and the use of splints.

We would not suggest abandoning well established principles of surgical treatment on so little evidence as these few cases present. We have done with pyarthrosis what we are doing with pneumococcic hydrothorax; namely, to depend on specifics and on early tapping for drainage while watching the patient as a whole, i. e. taking daily blood cultures and making frequent examinations for new foci of suppuration and for intoxication by the drug employed. With specific treatment there is little danger of a recurrence of pneumococcemia if the purulent focus is improving. This is consistent with the present concept of the action of the sulfonamides. Such management provides a maximum of the drug that is bacteriostatic and drains the local area where inhibiting substances may develop from tissue necrosis or abscess.

In case 4 incision and drainage were employed together with serum, this being in 1937 before the sulfonamides were used. Our series is arranged chronologically from 1936 to 1942 to represent the progressive change from the usual surgical incision and drainage to the use of serum and sulfonamides as they became available.

Patient 2 received no treatment because she was considered, at the age of 90, too old to be given serum, this being in 1936. Patient 3 was untreated because he came too late for specific treatment as given in 1937.

The decisions about drainage or tapping were easily made by following the principle of tapping for diagnosis as soon as the disease was suspected and continuing to tap to provide drainage as often as any fluid reaccumulated. Splints were used to immobilize the joints as long as there was fever.

Sulfathiazole was used oftener than other sulfonamides. Serum alone was used five times. In only 2 cases did we use combined drug and serum therapy. In but 1 instance did we use agglutination tests or skin tests to decide matters of dosage. We were guided by temperature and local signs mainly. Theoretically, serum and a sulfonamide compound should be used together as in the treatment of influenzal meningitis, but our series does not suggest such a method to be superior. We think that serum should be given to any patient who is not doing well with the drug alone or who has a positive blood culture late in the course of pneumonia.

The complication of pyarthrosis seemed to prolong the fever of pneumonia in several instances, but usually it did not. We have one example of delayed resolution but not beyond such delay as might occur in uncomplicated pneumonia. Pyarthrosis unassociated with pneumonia when treated with drugs responds in about the same manner as does gonococcic arthritis.

RESULTS

Three of the 11 patients died; 2 were given no treatment for the reasons stated and 1 must be regarded as having had too little serum (80,000 units of horse serum in case 1) and no drug because there was none.

In the usual sense of assessing specific treatment, there was no treatment failure. This we think noteworthy because the usual prognosis has been "always grave."

Bulkley in 1914 found from the collected literature a fatality rate of 24 per cent for single joint involvement and 72 per cent for multiple. We think the fatality rate should be that of uncomplicated pneumonia.

During the acute stage of the disease all the cases were seen by consultants from orthopedic or surgical services, who concurred in our form of treatment except in case 4, which was treated by surgeons. Physical therapy was not needed to bring the joints back to normal function except in one instance (case 4).

A follow-up study of these cases shows perfect functional results except in case 4 treated with incision and drainage. This knee seventeen months later showed good function for ordinary work but with some limitation of motion.

Cases are reported briefly herewith:

REPORT OF CASES

CASE 1.—L. B., a Negro aged 35, was admitted on the fifth day of his disease with bilateral lobular pneumonia due to pneumococcus type II. The white blood cell count was above 34,000 and blood culture was sterile. On the second hospital day and the fifth day of arthritis 5 cc. of purulent fluid which yielded pneumococcus type II was aspirated from his elbow. An insufficient amount (80,000 units) of horse serum was administered the fourth hospital day with a subsequent temperature drop to 99 F., but death occurred four days later. Permission for autopsy was not granted, but acute pericarditis seemed quite likely. Blood cultures remained negative.

CASE 2.—A. B., a Negro woman aged 90, was admitted with bacteremia and with arthritis of fourteen days' duration and

lobular pneumonia of three days' duration, both due to pneumococcus type XI. The white blood cell count was 11,000. Aspiration from her knee yielded 30 cc. of purulent fluid containing pneumococcus type XI on the second hospital day. She received no specific therapy because of her age and died on the third hospital day with bacteremia, meningitis and endocarditis, confirmed by autopsy.

CASE 3.—D. W., a white man aged 41 with pneumonia of the left lower lobe due to pneumococcus type V, was admitted with bacteremia and signs of endocarditis on the fifth day of his disease. On seven occasions his blood culture was positive for pneumococcus type V. The knee and acromioclavicular joints were aspirated on the tenth day, yielding 70 cc. and 5 cc. respectively of fluid which was purulent and yielded pneumococcus type V on culture. No specific was used for treatment because of the advanced stage of his disease. The temperature remained above 102 F., the white blood cell count was above 12,000 and he died, probably of endocarditis, on the eleventh hospital day. Permission for autopsy was not obtained.

CASE 4.—H. F., a white man aged 39 with pneumonia of the right upper lobe due to pneumococcus type I, was admitted with pneumococcic bacteremia on the fourth day of the disease. Eighty cc. of purulent fluid was removed from the knee on the second hospital day and 70 cc. was removed on the third hospital day. Cultures yielded pneumococcus type I. He received a total of 120,000 units of horse serum, and on the fifth day the joint was drained of 250 cc. of thick, creamy pus and then irrigated. Culture of this pus again revealed pneumococcus type I. The white blood cell count up to the tenth day remained above 23,000, but his temperature gradually fell from that of 105 F. on admission to normal when discharged as entirely recovered on the eighteenth day.

CASE 5.—J. J., a Negro girl aged 16 months, entered with pneumonia of the right upper lobe due to pneumococcus type VI. On the fourth hospital day (the sixth day of disease) 15 cc. of purulent fluid obtained from her ankle contained pneumococcus type VI. A subsequent tap was also positive. She had two positive blood cultures subsequent to her initial joint aspiration. Treatment consisted of 1,250 units of pneumococcus type VI serum and irrigation and drainage with a cast applied on the fifth day. Blood culture was negative when taken three days later. The white blood cell count of 23,100 and the elevated temperature gradually fell to normal, whereupon she was discharged as recovered on her twentieth hospital day.

CASE 6.—R. T., a white boy aged 4 years, was admitted with bronchopneumonia of two weeks' duration and arthritis of four days' duration due to pneumococcus type VI. This followed an attack of pertussis. His white blood cell count was 38,500, temperature was 104 F. and blood culture was positive for pneumococcus type VI. Four cc. of purulent exudate was aspirated from the ankle on the second hospital day, 2 cc. of thin, bloody fluid on the sixth day and 2 cc. of yellow pus on the eighth day. Cultures of each grew pneumococcus type VI. He received a total of 92,500 units of serum on the third and fourth days. He responded to the serum so that his temperature gradually fell to normal. After a few days of serum sickness he was discharged as recovered.

CASE 7.—J. W., a Negro aged 37, entered with pneumonia of the left lower lobe of one day's duration due to pneumococcus type VIII. Only the admission blood culture was positive. The knee was aspirated of 20 cc. of yellow-green fluid twice, but cultures were sterile. Twelve Gm. of sulfamethylthiazole was administered each day for six days. The drug level in the blood ranged above 4 mg. per hundred cubic centimeters and the white blood cell count between 5,000 and 16,000. Gradually his temperature fell to normal, and he was discharged on the twentieth day.

CASE 8.—T. R., a white man aged 66, entered with a gastric complaint due to a malignant growth and hematemesis. After several transfusions he was found on the eighteenth day to have arthritis of the knee. His blood stream was sterile, but 2 cc. of amber colored fluid obtained from the knee yielded pneumococcus type III. Subsequent taps yielded 60 cc. and 50 cc. of cloudy yellow fluid, which was sterile. A total of 26 Gm. of sulfapyridine was given over a period of seven days, with a subsequent fall in temperature and recovery of the knee.

CASE 9.—O. S., a Negro aged 37, was admitted with pneumonia of the right lower lobe of seven days' duration and bacteremia due to pneumococcus type V. The bacteremia, present on admission, cleared promptly, but on the fourth day arthritis developed. Cultures of 30 cc. of moderately thick yellow fluid aspirated from the knee and 2 cc. of thick pyosanguineous exudate from a sternoclavicular joint were sterile. He received 200,000 units of pneumococcus type V serum on the second hospital day; he first received sulfapyrazine and then sulfathiazole in doses of 6 Gm. a day until two days before discharge. He maintained an average blood level of 2 mg. per hundred cubic centimeters. The white blood cell count remained elevated around 18,000 until the twelfth day. The temperature gradually fell from 104 F., then rose to 103 F. again and subsequently dropped to normal. He was discharged on the twenty-seventh day as fully recovered.

CASE 10.—S. H., a Negro aged 71, entered the hospital complaining only of a sore knee of one week's duration. On admission a diagnostic tap revealed 60 cc. of purulent fluid containing pneumococcus type VII; 50 cc. of purulent fluid aspirated on the seventh day was again positive. In eight days he received a total of 9 Gm. of sulfadiazine and later 26 Gm. of sulfathiazole with drug levels as high as 9.1 mg. per hundred cubic centimeters. The temperature was 100 F. on admission, rose to 102 F. and gradually fell to normal in fourteen days. The white blood count rose to 17,100 at the time of the temperature spike. He left the hospital on his eighteenth day with some limitation in flexion.

CASE 11.—E. B., a Negro woman aged 39, entered the hospital with pneumonia of the right lower lobe and bacteremia due to pneumococcus type VIII. Subsequent blood cultures were sterile, but a diagnostic aspiration of 1 cc. of gelatinous material from the ankle on the second hospital day revealed pneumococcus type VIII. The joint fluid was again positive on the eighth day, when 6 cc. was removed, but became sterile, as shown by subsequent taps—one of 30 cc. of serous bloody fluid, another of 4 cc. of bloody, watery fluid. In twenty-one days she received a total of 58 Gm. of sulfathiazole followed by 60 Gm. of sulfadiazine. Sulfadiazine was substituted because of apparent sulfathiazole intoxication. On the fifth day she received 75,000, on the seventh 100,000 and on the ninth 80,000 units of specific serum, a total of 255,000 units, because she was not fever free and joint cultures were still positive. With this treatment and with blood levels over 4 mg. per hundred cubic centimeters, her white blood cell count dropped from 41,000 to 10,300 and her joint became better. She "signed out" of the hospital as fully recovered of her joint difficulty but with her pneumonia still not completely resolved. She was seen a month later and was entirely well.

SUMMARY

The 11 cases of pneumococcic pyarthrosis presented show the results of conservative specific treatment.

Three patients died, 2 receiving no specific treatment and the third receiving serum in insufficient amounts.

Eight patients recovered completely.

With specific sulfonamide or serum treatment, repeated aspiration is recommended. Surgical drainage was found unnecessary.

Emotional Thinking.—At the basis of most immature attitudes will be found "emotional thinking," which consists primarily of jumping to conclusions because of the undue influence of wishes or fears, or because of lack of training in the proper way of thinking. . . . Emotion is an integral part of the bodily process, and the expression of the basic drives and energy of the organism. . . . Just as emotion without the direction and control of the intellect defeats itself by its own excesses, so the intellect without the driving force of emotion remains sterile, incapable of accomplishment. . . . Logical thought or reason is direct, clear, influenced only by facts, and based on premises arrived at objectively and understandingly.—Kraines, Samuel H.: The Therapy of the Neuroses and Psychoses, Philadelphia, Lea & Febiger, 1943.

Clinical Notes, Suggestions and New Instruments

MONOCULAR MYASTHENIA GRAVIS

SIGMUND S. WINTON, PH.D., M.D., CHICAGO

A recent report by Moore[1] has directed attention to the fact that occasional cases of myasthenia gravis exhibit no symptoms or signs other than those referable to the ocular apparatus. Coincidentally, he raises considerable speculation as to the frequency with which this monosymptomatic form of myasthenia is erroneously diagnosed as neurosyphilis, organic oculomotor palsy or some similar neurologic condition. Although ocular signs and symptoms are numbered among the common clinical features of myasthenia, their correct etiologic basis is often overlooked until other unmistakable and more widespread concomitants have made their appearance. Two cases illustrative of this condition, i. e. monocular myasthenia gravis, are described. In 1 of these neurosyphilis had been suspected as the etiologic factor. In the other, in which diplopia was complained of, the clinical picture, in addition to ptosis, suggested the diagnosis of oculomotor nerve paralysis. Moore also cites 1 case seen several years earlier in conjunction with Winkelman.[2] Diagnosis of neurosyphilis and a posttraumatic state had been made and both antisyphilitic treatment and operative procedures were carried out before the correct nature of the condition was brought to light. These instances further serve to illustrate the difficulties of accurate diagnosis by observation alone. Electromyographic and electroergographic methods and other tests such as the Jolly reaction can be used to ascertain the state of skeletal muscle function. However, as Moore points out, all these methods are either unsuitable for testing ptosis or require cumbersome or elaborate apparatus. Under such circumstances, practicability dictates the use of a simpler and more reliable test. That prostigmine is valuable as a diagnostic agent as well as in treatment is illustrated in the case reported here.

Fig. 1.—Appearance of patient before treatment with prostigmine methylsulfate.

REPORT OF CASE

History.—M. T., a girl aged 16 years, complained of drooping of the left upper eyelid of sudden onset. She stated that three weeks prior to this event she had been suffering from a moderately severe head and chest cold, which cleared up with medication and rest. For about ten days she had felt her usual self, then one morning awoke to find the upper left eyelid drooping and almost covering the pupil. She experienced no unusual general fatigue but noticed that she was unable to raise the eyelid even on extreme effort. On the advice of a physician she applied hot fomentations to the left side of the face and continued this treatment for about two weeks without any sign of improvement. The patient had no difficulty in chewing her food, in swallowing or in phonation, nor was there any history of hysteria, temperamentality or emotional upset. Her appetite was good and her diet well balanced. Her weight, which had varied little in the past year, was 103 pounds (47 Kg.). She did not complain of discomfort in her neck or chest or of chronic cough or sputum. Exercise caused no unusual fatigue of the muscles of the extremities.

Fig. 2.—Same patient one month later while under treatment with prostigmine methylsulfate.

Physical Examination.—On examination two weeks after the onset of this condition, the patient appeared well nourished and well developed. There was a pronounced ptosis of the left upper eyelid, which could not be raised even with the utmost effort (fig. 1). The lower border of the lid crossed the center of the pupil. There were no ophthalmoplegia and no impairment of visual acuity. The pupils were round and equal on both sides and reacted to light and in accommodation. There was no abnormal facial expression; she was able to laugh, frown and wrinkle her forehead with ease. The gag reflex was present and there was no evidence of impairment of either chewing or swallowing. There was no cervical adenopathy nor any evidence of thymic enlargement. The chest was well developed and the heart and lungs were normal. The abdomen was scaphoid in contour. Careful examination of the extremities revealed no superficial abnormalities, atrophy, hypertrophy or fibrillary twitchings. The power of the muscles was good and the deep reflexes active and equal on the two sides.

Laboratory Examination.—Hemoglobin was 90 per cent, red blood cells numbered 5,000,000 and white blood cells 7,300, with lymphocytes 40 per cent, polymorphonuclears 59 per cent, eosinophils 1 per cent and basophils 0. Urinalysis showed absence of albumin and sugar. Microscopic examination was negative. The blood Wassermann reaction also was negative. Ergographic tests were omitted as there was no evidence of general muscular weakness. When 1 cc. of prostigmine methylsulfate (1:2,000) was injected subcutaneously as a therapeutic test a definite response was obtained within fifteen minutes. The eyelid began to fibrillate slightly and then gradually began to rise until the lower border reached the upper edge of the pupil.

Treatment.—At the beginning of treatment the patient was given one injection of prostigmine methylsulfate 1:2,000 twice weekly. Following each injection the ptosis disappeared and

Hoffmann-La Roche, Inc., made generous contributions of prostigmine in the treatment of this case.

1. Moore, M. T.: Monocular Myasthenia Gravis; Prostigmine Methylsulfate as a Differential Diagnostic Agent, Arch. Ophth. **26:** 619 (Oct.) 1941.

2. Winkelman, N. W., and Moore, M. T.: Prostigmine in the Treatment of Myasthenia Gravis and Muscular Dystrophy, Arch. Neurol. & Psychiat. **37:** 237 (Feb.) 1937.

the eyelid regained its normal tone and power (fig. 2), which effects lasted for only a few hours. In order to increase the concentration of prostigmine in the blood, prostigmine bromide tablets were given in 15 mg. doses three times daily in addition to the weekly hypodermic injection. The lid remained constantly elevated and had good tone and power but occasionally fibrillated and appeared overcompensated. When the total daily dose of the bromide was dissolved in water and taken in smaller but more frequent quantities throughout the day, fibrillation was less often seen. On several occasions the patient complained of headaches and abdominal cramps. After several months on this management the patient developed a tolerance to prostigmine and at various occasions noticed slight drooping of the lid. Guanidine hydrochloride in the dose of 0.1 Gm. three times daily was then substituted for prostigmine, but the results were not satisfactory. Ephedrine sulfate and potassium chloride also failed to produce any improvement in the ptosis. The best results were obtained with a combination of 15 mg. of prostigmine bromide and 0.1 Gm. of guanidine hydrochloride taken three times daily with meals. Under this regimen the patient remained comfortable, active and free from ptosis. After four months the guanidine was omitted and the dose of prostigmine gradually reduced, until the patient was taking one tablet (15 mg.) every third day. Her condition appeared to progress favorably for about one month, after which the lid gradually began to show signs of weakness and slight ptosis. After combined therapy with prostigmine and guanidine was reinstituted, however, all symptoms remained in abeyance. For the past eighteen months she has been enjoying excellent health.

COMMENT

This case affords an illuminating example of strict localization of myasthenic signs. Whether or not, lacking specific therapy, more widespread involvement would have occurred is problematic. A review of the literature shows, however, that ocular abnormalities are often but the forerunners of the full fledged disease. The implications with respect to early diagnosis and treatment seem obvious.

The use of prostigmine for diagnostic purposes has been extensively studied by Viets, Schwab and Mitchell.[3] The test consists simply in the intramuscular injection of 1.5 mg. of prostigmine methylsulfate (plus 1/100 grain [0.00065 Gm.] of atropine sulfate) and the observation of the objective and subjective improvement at ten minute intervals for one hour. No apparatus is needed other than an ordinary hypodermic needle and syringe. The treatment of myasthenia by prostigmine methylsulfate and prostigmine bromide is a topic too well known to justify discussion here.

AN IMPROVEMENT IN CATHETER TECHNIC FOR CONTINUOUS CAUDAL ANESTHESIA

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Recently Adams and Lundy [1] described the catheter technic for continuous caudal anesthesia. The method they described involved the use of a 13 gage Love-Barker spinal needle and a number 5 ureteral catheter. We [2] have used this method in over 250 obstetric cases without any serious complications. There are, however, some objections: 1. The caliber of the needle is such that it is difficult to insert it into the caudal canal. 2. If there is difficulty in locating the caudal foramen and it becomes necessary to reinsert the needle, considerable trauma ensues. As a result, patients complain of soreness at the site of insertion during the first few days post partum.

Recently we have overcome this difficulty and simplified the technic considerably by employing a 15 gage needle with obturator and a number 4 ureteral catheter. It is much easier to insert a small caliber needle into the caudal canal. The 15 gage 3 inch needle is considerably smaller than the 13 gage. This difference in size stands out when the needles are placed side by side.

For obese persons or for patients with a small sacral foramen we use a special 18 gage needle 5½ inches long. This needle is hubless and was devised through the cooperation of Mr. Oscar Schwidetzky, manager of the research department of Becton, Dickinson & Co. We employ this needle in the difficult cases. After it is inserted, the 15 gage needle without the obturator is passed over it as a sleeve. The 18 gage needle is then removed. The number 4 ureteral catheter is inserted into the caudal canal through the 15 gage needle, which is withdrawn, leaving the catheter in place. A 25 gage hypodermic needle is inserted into the external end of the catheter, which is connected by an adaptor to an injection system similar to that described by Hingson and Edwards. The 15 gage needle can be used direct in over 75 per cent of cases, the hubless 18 gage needle being reserved for the difficult patient. We have employed this method in over 100 cases. It is notable that there are less complaints from patients with regard to soreness and irritation at the site of puncture.

The use of a number 4 ureteral catheter was reported by Manalan,[3] but he employed a 14 gage needle.

The catheter method obviates the danger of a broken needle, which can be a major complication.[4] Patients can move about freely and are more comfortable. We believe it will be the method of choice in obstetric cases in which continuous caudal anesthesia is employed.

The number 4 ureteral catheters can be obtained from the American Cystoscopic Company or the Bard Company, 79 Madison Avenue, New York City. They are boilable and can be used many times.

3. Viets, H. R., and Schwab, R. S.: Prostigmine in the Diagnosis of Myasthenia Gravis, New England J. Med. **213:** 1280 (Dec. 26) 1935. Viets, H. R., and Mitchell, R. S.: The Prostigmine Test in Myasthenia Gravis, ibid. **215:** 1064 (Dec. 3) 1936. Schwab, R. S., and Viets, H. R.: The Prostigmine Test in Myasthenia Gravis: Third Report, ibid. **219:** 226 (Aug. 18) 1938.

From the Department of Obstetrics, Syracuse University College of Medicine.

1. Adams, R. C.; Lundy, J. S., and Seldon, T. H.: Continuous Caudal Anesthesia or Analgesia: A Consideration of Technic, J. A. M. A. **122:** 152-158 (May 15) 1943.

2. Irving, F. R.; Lippincott, C. A., and Meyer, Frank: Continuous Caudal Anesthesia in Obstetrics, New York State J. Med. **43:** 1023-1029 (June 1) 1943.

3. Manalan, S. A.: Caudal Block Anesthesia in Obstetrics, J. Indiana M. A. **35:** 564-565 (Oct.) 1942.

4. Block, Nathan, and Rotstein, Morris: Continuous Drip Caudal Anesthesia in Obstetrics, J. A. M. A. **122:** 582 (June 26) 1943.

The preceding articles in this series were published in THE JOURNAL May 31, 1913, p. 1702; May 9, 1914, p. 1473; May 17, 1915, p. 1322; April 22, 1916, p. 1305; March 17, 1917, p. 845; March 16, 1918, p. 777; April 5, 1919, p. 997; March 6, 1920, p. 672; March 26, 1921, p. 860; March 25, 1922, p. 890; March 10, 1923, p. 691; Feb. 2, 1924, p. 389; March 14, 1925, p. 813; March 27, 1926, p. 948; April 9, 1927, p. 1148; May 19, 1928, p. 1624; May 18, 1929, p. 1674; May 17, 1930, p. 1574; May 9, 1931, p. 1576; April 30, 1932, p. 1550; May 13, 1933, p. 1491; May 19, 1934, p. 1677; June 8, 1935, p. 2093; June 6, 1936, p. 1983; June 19, 1937, p. 2118; July 30, 1938, p. 414; May 13, 1939, p. 1941; May 25, 1940, p. 2103; Jan. 17, 1942, p. 222, and Aug. 8, 1942, p. 1188.

Special Article

TYPHOID IN THE LARGE CITIES OF THE UNITED STATES IN 1942

THIRTY-FIRST ANNUAL REPORT

A communication was addressed to the health officer of each of the cities, requesting the number of deaths from typhoid, excluding paratyphoid, both among residents and among nonresidents as recorded for 1942. In addition to the tendency for many cities to keep no data on reallocations for residents there was observed a distinct carelessness on the part of some health officials to submit accurate and complete figures. In many instances the number of cases was given and only the challenge of the reviewer brought forth the data requested. For other cities multiple inquiries brought forth irreconcilable replies. Too frequently the answer was left to a subordinate employee, although there is evidence that in the largest cities the health officer has established a routine whereby he gives final approval to statistical data released by his department. It is recommended that the smaller cities follow this excellent example. A few health officers seem to have no knowledge of how many typhoid deaths have occurred in their community and this information can be secured

only from the state health department. The possession of basic data seems paramount to the establishment and maintenance of adequate local health services.

Each health officer was asked to record an estimate of population for 1942. Many are continuing to use the 1940 census figures; others have prepared local estimates using ration book data or adjustments which are questionable. Except for Washington, the Bureau of Census has prepared no population estimates for cities since the 1940 census. Registration data for War Ration Book One was reported only on a county basis and similar estimates for cities are not available. Since no official figures are available for any date subsequent to that of the federal census, it has again been deemed advisable to employ the populations determined by this uniform tabulation. It is recognized that in areas of concentration of military and industrial activities a slight error will result, and some city and group rates may be a little too high and even too low.

Paratyphoid has again been excluded. Special note has been made of cities in which all deaths occur among nonresidents. In addition to the fifty-three cities enumerated on the honor roll in table 10, ten cities (Birmingham, Dallas, Indianapolis, Jacksonville, Knoxville, Nashville, Pittsburgh, San Diego, St. Louis, Utica) are qualified for such acclaim but have been charged with typhoid deaths among nonresidents cared for in these cities. In nine other cities (Atlanta, Baltimore, Buffalo, Cincinnati, Jersey City, Kansas City, Kan., Louisville, New Orleans, Washington) more than one third of the reported deaths were stated to have been among nonresidents. One city with more than one million inhabitants (Detroit) records no death from typhoid.

The number of cities with no typhoid death during the past two or more years has increased from twenty-five in 1941 to thirty-one in 1942 (table 9). Fort Wayne continues to head the list with no death in eight years. South Bend has maintained its excellent record and has been without a death for seven years. Fall River, Lynn and New Bedford report no death in six years; Cambridge and Lowell, no death in five years.

The New England cities (table 1) (population 2,579,152) have the lowest group rate (0.12) but are closely followed by the East North Central cities (0.14) and the Middle Atlantic cities (0.15). The West North Central cities (0.18) are not far behind. Eleven of the New England cities (there were eight in 1941, ten in 1940, eleven in 1939) report no death from typhoid in 1942 (table 1). Cambridge, Fall River, Hartford, Lowell, Lynn, New Bedford, Somerville and Springfield have maintained their ranking of 1941, while Bridgeport, New Haven and Worcester have been added to the honor roll. Springfield reports no death among residents during the past nine years, Hartford none for five years. While in 1940 one half of the eighteen cities recording no deaths from typhoid during a two year period were to be found among the New England cities and in 1941 one third (eight among twenty-five) were from these cities, in 1942 one fourth (eight among thirty-one) were from this group. This in no manner subtracts from the outstanding record of the New England cities but rather does it show the

TABLE 1.—*Death Rates of Fourteen Cities in New England States from Typhoid per Hundred Thousand of Population*

	1942	1941	1936-1940	1931-1935	1926-1930	1921-1925	1916-1920	1911-1915	1906-1910
Cambridge	0.0	0.0	0.2*	0.8	2.1	4.3	2.5	4.0	9.8
Fall River	0.0	0.0	0.2	0.2	2.2	2.3	8.5	13.4	13.5
Lynn	0.0	0.0	0.2	0.2	1.5	1.6	3.9	7.2	14.1
Springfield	0.0	0.0	0.3*	1.1†	0.4	2.0	4.4	17.6	19.9
New Bedford	0.0	0.0	0.4	1.1	1.5	1.7	6.0	15.0	16.1
Lowell	0.0	0.0	0.4	1.2	2.6	2.4	5.2	10.2	13.9
Hartford	0.0	0.0	0.5	1.0†	1.3	2.5	6.0	15.0	19.0
Somerville	0.0	0.0	0.6	0.4	1.3	1.6	2.8	7.9	12.1
Worcester	0.0	0.5	0.2*	0.5*	1.0	2.3	3.5	5.0	11.8
New Haven	0.0	0.6	1.0	0.7†	0.6	4.4	6.8	18.2	30.8
Bridgeport	0.0	0.7	0.4	0.3	0.5	2.2	4.8	5.0	10.3
Boston	0.1	0.1	0.3†	0.6	1.2	2.2	2.5	9.0	16.0
Providence	0.4	0.4*	0.6	1.1†	1.3	1.8	3.8	8.7	21.5
Waterbury	1.0	1.0	0.2	0.4	1.2	1.0	8.0	18.8	....

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.

TABLE 2.—*Death Rates of Eighteen Cities in Middle Atlantic States from Typhoid per Hundred Thousand of Population*

	1942	1941	1936-1940	1931-1935	1926-1930	1921-1925	1916-1920	1911-1915	1906-1910
Yonkers	0.0	0.0	0.3	0.7	0.5	1.7	4.8	5.0	10.3
Newark	0.0	0.0	0.3	0.4	0.9	2.3	3.3	6.8	14.6
Scranton	0.0	0.0	0.3	1.4	1.8	2.4	3.8	9.3	31.5
Erie	0.0	0.0	0.7†	1.2	0.9	2.3	6.9	49.0	46.6
Albany	0.0	0.0	1.2†	1.2	1.8	5.6	8.9	18.6	17.4
Trenton	0.0	0.0	1.4†	1.1	2.1	8.2	8.6	22.3	28.1
Rochester	0.0	0.3	0.3†	0.4	1.7	2.1	2.9	9.6	12.8
Paterson	0.0	0.7*	0.7†	0.9	1.0	3.3	4.1	9.1	19.3
Camden	0.0	0.8	1.4†	2.7	4.4	5.9	4.9	4.5	4.0
Reading	0.0	0.9	0.5	0.4	1.6	6.0	10.0	31.9	42.0
Elizabeth	0.0	0.9	0.5	0.9	1.6	2.4	3.3	8.0	16.6
Pittsburgh	0.1*	0.4	0.7	0.9	2.4	3.9	7.7	15.9	65.0
New York	0.1	0.2	0.3	0.8	1.3	2.6	3.2	8.0	13.5
Philadelphia	0.4	0.4	0.8	0.9	1.1	2.2	4.9	11.2	41.7
Buffalo	0.5†	0.9	0.1	0.6	2.7	3.9	8.1	15.4	22.8
Syracuse	0.5	0.5*	0.3*	0.8	0.8	2.3	7.7	12.3	15.6
Jersey City	0.7†	0.0	0.6	0.3	0.9	2.7	4.5	7.2	12.6
Utica	1.0*	1.0	0.2*	0.2	1.1	3.3#	....	....	....

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

TABLE 3.—*Death Rates of Ten Cities in South Atlantic States from Typhoid per Hundred Thousand of Population*

	1942	1941	1936-1940	1931-1935	1926-1930	1921-1925	1916-1920	1911-1915	1906-1910
Wilmington	0.0	0.0	0.5	1.5	3.1	4.7	25.8#	23.2#	33.0
Norfolk	0.0	0.7	1.1†	3.3	2.2	2.8	8.8	21.7	42.1
Charlotte	0.0	1.0	1.6†	2.5	...	...	....	....	....
Baltimore	0.3†	0.7†	0.9†	1.4	3.2	4.0	11.8	23.7	35.1
Washington	0.3†	0.7†	1.1	2.2	2.8	5.4	9.5	17.2	36.7
Miami	0.6	1.2	2.4	2.0	3.5	...	....	....	....
Jacksonville	0.6*	2.9	2.3	1.6	4.4	...	....	....	....
Atlanta	1.0†	0.7*	2.1†	7.3	11.1	14.5	14.2	31.4	58.4
Richmond	2.0†	1.0†	2.5†	2.4	1.9	5.7	9.7	15.7	34.0
Tampa	4.6†	0.9*	0.6†	3.4	3.8	19.1	43.1#	....	....

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

TABLE 4.—*Death Rates of Nineteen Cities in East North Central States from Typhoid per Hundred Thousand of Population*

	1942	1941	1936-1940	1931-1935	1926-1930	1921-1925	1916-1920	1911-1915	1906-1910
South Bend	0.0	0.0	0.0	0.8	....	....	....	....	....
Fort Wayne	0.0	0.0	0.0	2.1	4.2	12.9	7.3	....	....
Grand Rapids	0.0	0.0	0.5†	0.2	1.0	1.9	9.1	25.5	29.7
Canton	0.0	0.0	0.4†	0.8	1.4	3.3	8.9	....	....
Akron	0.0	0.0	0.6†	0.9	1.5	2.4	10.6	21.0	27.7#
Gary	0.0	0.0	1.1	0.8	....	....	....	....	....
Evansville	0.0	0.0	1.2†	1.8	6.2	5.0	17.5	32.0	35.0
Milwaukee	0.0	0.2	0.1	0.2	0.8	1.6	6.5	13.6	27.0
Detroit	0.0	0.2	0.4	0.7	1.3	4.1	8.1	15.4	22.8
Youngstown	0.0	0.6*	0.7	1.2	1.1	7.2	19.2	29.5	35.1
Peoria	0.0	0.9	1.3†	0.9	0.2	3.7	5.7	16.4	15.7#
Dayton	0.0	0.9*	1.4	0.8	1.9	3.3	9.3	14.8	22.5
Chicago	0.1	0.1	0.3	0.4	0.6	1.4	2.4	8.2	15.8
Cleveland	0.2	0.2†	0.6	1.1	1.9	2.9	4.0	10.0	15.7
Indianapolis	0.3*	0.3*	1.2†	1.8	2.7	4.6	10.3	20.5	30.4
Columbus	0.3	0.3*	1.4†	1.9	2.1	3.5	7.1	15.8	40.0
Cincinnati	0.4†	0.2	1.1†	1.4	2.5	3.2	3.4	7.8	30.1
Toledo	0.4	0.4*	1.0†	1.2	3.0	5.8	10.6	31.4	37.5
Flint	2.6	0.7	1.3†	0.8	1.6	4.6	22.7	18.8	46.9

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

tendency for other cities to attain the high standards set by this group. Worcester, with the first death in 1941 among residents for eleven years, now returns to the honor roll; Bridgeport and New Haven, each with one resident death in 1941, also return to the honor roll. Bridgeport reported no deaths during the five year period 1935-1939. Boston reports one death among residents (the same as for 1941). For the fourteen New England cities there were but three deaths, all among residents, one each for Boston, Providence and Waterbury. The rate (0.12) is the lowest thus far attained by any group of cities (table 13). The New England cities regain first place, which position they held during the quinquennium 1936-1940.

Eleven of the large Middle Atlantic cities (there were eight in 1941, nine in 1940) report no death from typhoid in 1942 (table 2). Albany, Erie, Newark, Scranton, Trenton and Yonkers have maintained their ranking of 1941, while Camden, Elizabeth, Paterson, Reading and Rochester have been added to the honor roll. The Middle Atlantic cities have a group rate (0.15) which is but slightly higher than that of the New England and East North Central cities. It is much lower than the rates for 1941 (0.24), 1940 (0.27) and 1939 (0.37). Six cities (Albany, Erie, Newark, Scranton, Trenton, Yonkers) report no typhoid death during 1941 and 1942 (table 9), Yonkers none for four years, Erie, Newark and Scranton none for three years. After the passage of five years with but one death among residents in Buffalo it is stated that in 1942 there occurred three deaths, two among residents. Utica reports only one death among residents during the past eleven years, Erie one such death for eight years. For the first time Pittsburgh records no death among residents (there were three in 1941) and only one among nonresidents (there was but one resident death in 1933 and again in 1939). After a period of six years with no death among residents, Syracuse records one such death in 1942. Rochester reports but one death during the past three years. New York records a significant decrease in the number of deaths (five in 1942, all among residents; fourteen in 1941, thirteen among residents). It is stated that in Philadelphia there occurred seven deaths, all among residents. There were seven deaths in 1941 (five among residents) and twelve in 1940 (eleven among residents). Jersey City reports two deaths, one among residents. In the group as a whole (population 13,129,185) there were twenty deaths in 1942 compared with thirty-one in 1941, thirty-six in 1940 and forty-eight in 1939.

The rate (0.70) for the South Atlantic cities (table 3) (population 2,727,985) is lower than the rate of 1941 (0.88) and that of 1940 (0.73). In these cities there occurred nineteen deaths in 1942, twenty-four in 1941 and twenty in 1940. The number of deaths among residents has decreased from thirteen in 1941 to ten in 1942. Three cities (Charlotte, Norfolk, Wilmington) are on the honor roll, and it is stated that the one death in Jacksonville occurred among nonresidents. Five cities (Atlanta, Baltimore, Richmond, Tampa, Washington) report that one third or more of deaths were among nonresidents (one of three in Atlanta, two of three in Baltimore, two of four in Richmond, two of five in Tampa, one of two in Washington). Charlotte (no death in 1942) has been included in the group for the third time; however, for purposes of adequate comparison the figures for this city have been omitted in calculating rates for the group as a whole.

The East North Central cities (population 9,386,378) have lost first place, which rank they held in 1941 and back in 1938. Twelve (eleven exclusive of Gary) of the cities in this group (Akron, Canton, Dayton, Detroit, Evansville, Fort Wayne, Gary, Grand Rapids, Milwaukee, Peoria, South Bend, Youngstown) report no death from typhoid in 1942 (table 4). Gary was added to this group in 1940, but figures for this city have been omitted in determining rates for the group as a whole. The number of typhoid deaths decreased from nineteen

TABLE 5.—*Death Rates of Six Cities in East South Central States from Typhoid per Hundred Thousand of Population*

	1942	1941	1936-1940	1931-1935	1926-1930	1921-1925	1916-1920	1911-1915	1906-1910
Memphis	0.0	0.3*	4.0†	7.5	9.3	18.9	27.7	42.5	35.3
Chattanooga	0.0	0.8	0.9	5.8	8.0	18.6	27.2	35.8#	....
Louisville	0.6†	0.9†	0.9	2.8	3.7	4.9	9.7	19.7	52.7
Nashville	0.6*	1.2*	3.4†	5.7	18.2	17.8	20.7	40.2	61.2
Birmingham	0.7*	0.4	2.5†	4.1	8.0	10.8	31.5	41.3	41.7
Knoxville	1.8*	0.9*	3.8	6.0	10.7	20.8	25.3#	....	....

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

TABLE 6.—*Death Rates of Nine Cities in West North Central States from Typhoid per Hundred Thousand of Population*

	1942	1941	1936-1940	1931-1935	1926-1930	1921-1925	1916-1920	1911-1915	1906-1910
Duluth	0.0	0.0	0.2	1.0	1.1	1.7	4.4	19.8	45.5
Des Moines	0.0	0.0	1.3	2.5	2.4	2.2	0.4	15.9	23.7
Omaha	0.0	0.0	0.6	0.9	1.3	3.3	5.7	14.9	40.7
Minneapolis	0.0	0.2	0.2	0.8	0.8	1.9	5.0	10.6	32.1
Kansas City, Mo.	0.0	0.3	0.9†	1.6	2.8	5.7	10.6	16.2	35.6
St. Louis	0.1*	0.5†	0.7	1.6	2.1	3.9	6.5	12.1	14.7
St. Paul	0.3	0.0	0.3	0.7	1.4	3.4	3.1	9.2	12.8
Wichita	0.9	0.0	0.4	1.1	1.2	6.3	....	....	....
Kansas City, Kan.	1.6†	1.6*	1.0	1.0	1.7	5.0	9.4	31.1	74.5#

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

TABLE 7.—*Death Rates of Eight Cities in West South Central States from Typhoid per Hundred Thousand of Population*

	1942	1941	1936-1940	1931-1935	1926-1930	1921-1925	1916-1920	1911-1915	1906-1910
Tulsa	0.0	0.0	0.4	1.1	8.3	16.2#	....	....	....
Oklahoma City	0.0	0.0	2.6	4.3	7.4#	....	....	....	....
Dallas	0.3*	2.4†	2.7†	5.1	7.3	11.2	17.2	....	....
Houston	0.5	1.3	2.3	3.2	4.8	7.6	14.2	38.1	49.7#
Fort Worth	0.6	0.6*	2.1	4.5	5.9	6.1	16.3#	11.9	27.8
San Antonio	0.8	0.0	2.9	4.3	4.6	9.3	23.3	29.5	35.9
New Orleans	0.8†	2.2*	5.0†	9.6	9.9	11.6	17.5	20.9	35.6
El Paso	5.1†	4.1†	4.5	5.2	9.1	10.8	30.7	42.8	....

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

TABLE 8.—*Death Rates of Twelve Cities in Mountain and Pacific States from Typhoid per Hundred Thousand of Population*

	1942	1941	1936-1940	1931-1935	1926-1930	1921-1925	1916-1920	1911-1915	1906-1910
Seattle	0.0	0.0	0.2	0.7	2.2	2.6	2.9	5.7	25.2
Portland	0.0	0.0	0.3	0.8	2.3	3.5	4.5	10.8	23.2
Oakland	0.0	0.0	0.5†	1.2	1.2	2.0	5.8	8.7	21.5
Long Beach	0.0	0.0	0.5	0.5	1.1	2.1#	....	....	....
Salt Lake City	0.0	0.7*	0.3*	0.7	1.9	6.0	9.3	13.2	41.1
Sacramento	0.0	0.9*	1.5*	6.3	....	....	....	....	....
Tacoma	0.0	0.9	0.5	0.9	1.8	3.7	2.9	10.4	19.0
San Francisco	0.2	0.3†	0.4	0.8	2.0	2.8	4.6	13.6	26.3
San Diego	0.5*	0.5	0.8	1.3	1.0	1.6	7.9	17.0	10.8
Los Angeles	0.5	0.7†	0.7†	0.8	1.5	3.0	3.6	10.7	19.0
Spokane	0.8	0.0	1.2	1.0	2.2	4.4	4.9	17.1	50.3
Denver	0.9†	0.3*	1.4	1.7	2.6	5.1	5.8	12.0	37.5

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

(thirty-three in 1940) to thirteen (the rate from 0.35 in 1940 and 0.20 in 1941 to 0.14). Six cities (Akron, Canton, Evansville, Fort Wayne, Grand Rapids, South Bend) record no typhoid death during 1941 and 1942 (table 9), Fort Wayne none for eight years; South Bend none for seven years, Canton and Grand Rapids none for three years. Detroit seems thus far to be the largest city to pass through a year without a typhoid death, either among residents or among nonresidents. In 1941 there were four deaths in Detroit, three among residents. Indianapolis reports one death among nonresidents; Cincinnati records two deaths, one among residents. Grand Rapids extends her record to but two deaths among residents for more than twelve years. No death among residents of Canton is recorded during the past six years. Chicago reports two deaths (three in 1941) among residents. Cleveland also records two deaths among residents, Columbus one such death. It is stated that four deaths among residents occurred in Flint and one such death in Toledo.

TABLE 9.—*Thirty-One Cities with No Typhoid Deaths in 1941 and 1942* #

Akron	Grand Rapids ‡	Portland ‡
Albany	Hartford †	Scranton ‡
Cambridge **	Long Beach	Seattle ‡
Canton ‡	Lowell **	Somerville
Des Moines ‡	Lynn *	South Bend ¶
Duluth †	Newark ‡	Springfield †
Erie ‡	New Bedford *	Trenton
Evansville	Oakland	Tulsa ‡
Fall River *	Oklahoma City	Wilmington †
Fort Wayne ‖	Omaha	Yonkers †
Gary		

‖ No typhoid deaths in eight years.
¶ No typhoid deaths in seven years.
* No typhoid deaths in six years.
** No typhoid deaths in five years.
† No typhoid deaths in four years.
‡ No typhoid deaths in three years.
# Thirty without Gary.

TABLE 10.—*Death Rates from Typhoid in 1942*

Honor Roll: No Typhoid Deaths (Fifty-Three Cities)#

Akron	Grand Rapids	Portland
Albany	Hartford	Reading
Bridgeport	Kansas City, Mo.	Rochester
Cambridge	Long Beach	Sacramento
Camden	Lowell	Salt Lake City
Canton	Lynn	Scranton
Charlotte	Memphis	Seattle
Chattanooga	Milwaukee	Somerville
Dayton	Minneapolis	South Bend
Des Moines	Newark	Springfield
Detroit	New Bedford	Tacoma
Duluth	New Haven	Trenton
Elizabeth	Norfolk	Tulsa
Erie	Oakland	Wilmington
Evansville	Oklahoma City	Worcester
Fall River	Omaha	Yonkers
Fort Wayne	Paterson	Youngstown
Gary	Peoria	

First Rank: From 0.1 to 1.9 Deaths per Hundred Thousand (Thirty-Nine Cities)

Boston	0.1	Cincinnati	0.4†	Nashville	0.6*
Chicago	0.1	Philadelphia	0.4	Birmingham	0.7*
New York	0.1	Providence	0.4	Jersey City	0.7†
Pittsburgh	0.1*	Toledo	0.4	New Orleans	0.8†
St. Louis	0.1*	Buffalo	0.5†	San Antonio	0.8
Cleveland	0.2	Houston	0.5	Spokane	0.8
San Francisco	0.2	Los Angeles	0.5	Denver	0.9†
Baltimore	0.3†	San Diego	0.5*	Wichita	0.9
Columbus	0.3	Syracuse	0.5	Atlanta	1.0†
Dallas	0.3*	Fort Worth	0.6	Utica	1.0*
Indianapolis	0.3*	Jacksonville	0.6*	Waterbury	1.0
St. Paul	0.3	Louisville	0.6†	Kansas City, Kan.	1.6†
Washington	0.3†	Miami	0.6	Knoxville	1.8*

Second Rank: From 2.0 to 5.1 (Four Cities)

Richmond	2.0†	Tampa	4.6†
Flint	2.6	El Paso	5.1†

* All typhoid deaths are stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Fifty without Charlotte, Gary and Sacramento.

The six cities (table 5) in the East South Central group (population 1,286,747) again show a continuing decrease in the death rate (0.54 in 1942, 0.70 in 1941, 2.09 in 1940, 2.58 in 1939). Especially impressive is the fact that there was but one death among residents; the total of seven deaths includes six among nonresidents. The effect of hospitalizing cases from surrounding rural areas remains evident. Two cities (Chattanooga and Memphis) report no deaths among either residents or nonresidents and appear on the honor roll. The two deaths each in Birmingham and Knoxville as well as the one death in Nashville were stated to be among nonresidents. The single resident death occurred in Louisville, which city reports two deaths in 1942 (three in 1941, two among residents). Especially noteworthy is the decrease in Memphis from fifty-eight deaths (twenty-seven among residents) during the five year period 1936-1940 (an average of nearly twelve deaths a year) to no death in 1942. Knoxville reports no death among residents during the past two years.

The West North Central cities (population 2,716,484) show a decrease in the number of deaths from eight to five; three of the five were among residents. The death rate declined from 0.29 in 1941 (0.41 in 1940) to 0.18 in 1942. Five cities (Des Moines, Duluth, Kansas City, Mo., Minneapolis, Omaha) record no death and St. Louis reports one death among nonresidents. Wichita after no death for five years now reports one among residents; St. Paul also records such a death. Three cities (Des Moines, Duluth, Omaha) report no typhoid death during 1941 and 1942 (table 9), Duluth none for four years, Des Moines none for three years. Kansas City, Kan., records two deaths, one among nonresidents. St. Louis establishes a new record with no death among residents (there were two such deaths in 1941 in addition to two among nonresidents).

The eight cities of the West South Central group (table 7) (population 2,048,692) again report a decided reduction in the death rate (2.00 in 1940, 1.37 in 1941, 0.73 in 1942). The actual number of deaths decreased from twenty-eight (forty-one in 1940) to fifteen. Of the fifteen deaths in this group of cities, six were among nonresidents (seventeen of twenty-eight in 1941). Two cities (Oklahoma City, Tulsa) record no death and Dallas reports one death among nonresidents. Tulsa reports no death for three years. Two cities (El Paso, New Orleans) record one third or more deaths among

TABLE 11.—*Number of Cities with Various Typhoid Death Rates*

	No. of Cities	10.0 and Over	5.0 to 9.9	2.0 to 4.9	1.0 to 1.9	0.1 to 0.9	0.0
1906-1910	77	75	2	0	0	0	0
1911-1915	79	58	19	2	0	0	0
1916-1920	84	22	32	30	0	0	0
1921-1925	80	12	17	48	12	0	0
1926-1930	92	3	10	30	37	12	0
1931-1935	93	0	6	17	28	42	0
1930	93	2	6	30	23	22	10
1931	93	2	6	23	28	22	12
1932	93	1	7	13	29	29	14
1933	93	0	7	18	19	33	16
1934	93	0	9	11	27	23	23
1935	93	0	7	15	18	29	24
1936	93	0	3	15	21	36	18
1937	93	0	1	13	26	26	27
1938	93	0	3	13	14	34	29
1939	93	0	3	7	17	32	34
*1940	93	0	0	12	12	30	39
*1941	93	0	0	4	7	46	36
*1942	93	0	1	3	5	34	50

* Charlotte, Gary and Sacramento omitted.

nonresidents. Of five deaths in El Paso, two were among nonresidents; three out of four in New Orleans. Houston and San Antonio each report two deaths among residents, Fort Worth one such death. This group of cities continues to have the highest group rate

TABLE 12.—*Total Typhoid Rate for Seventy-Eight Cities, 1910-1942* *

	Population	Typhoid Deaths	Typhoid Death Rate per 100,000
1910	22,573,435	4,637	20.54
1911	23,211,341	3,950	17.02
1912	23,835,399	3,132	13.14
1913	24,457,989	3,285	13.43
1914	25,091,112	2,781	11.08
1915	25,713,346	2,434	9.47
1916	26,257,550	2,191	8.34
1917	26,865,408	2,016	7.50
1918	27,086,696†	1,824†	6.73
1919	27,735,083†	1,151†	4.15
1920	28,244,878	1,088	3.85
1921	28,859,062	1,141	3.95
1922	29,473,246	963	3.26
1923	30,087,430	950	3.16
1924	30,701,614	943	3.07
1925	31,315,598	1,079	3.44
1926	31,929,782	907	2.84
1927	32,543,966	648	1.99
1928	33,158,150	628	1.89
1929	33,772,334	537	1.59
1930	34,410,235	554	1.61
1931	34,508,750	563	1.63
1932	34,607,505	442	1.28
1933	34,708,945	423	1.22
1934	34,833,650	413	1.19
1935	35,005,351	348	0.99
1936	35,196,325	337	0.96
1937	35,386,380	289	0.82
1938	35,578,011	257	0.72
1939	35,767,022	232	0.65
1940	35,895,638	172	0.48
1941	35,895,638††	123	0.34
1942	35,895,638††	83	0.23
Rates for Ninety-Three Cities			
1935	37,025,179	385	1.04
1936	37,241,414	366	0.98
1937	37,459,339	324	0.86
1938	37,680,155	298	0.79
1939	37,900,354	259	0.68
1940	38,060,662	190	0.50
1941	38,060,662††	141	0.37
1942	38,060,662††	95	0.25

* The following fifteen cities are omitted from this table because data for the full period are not available: Canton, Chattanooga, Dallas, Fort Wayne, Jacksonville, Knoxville, Long Beach, Miami, Oklahoma City, South Bend, Tampa, Tulsa, Utica, Wichita, Wilmington.
† Data for Fort Worth lacking.
†† 1940 census figures used.

(0.73), but this compares most favorably with the New England rate of ten years ago (0.70 for 1931-1935) and is quite a contrast to the group's own rate for the same quinquennial period (5.36).

TABLE 13.—*Total Typhoid Death Rate per Hundred Thousand of Population for Ninety-Three Cities According to Geographic Divisions*

	Population *	Typhoid Deaths		Typhoid Death Rates				
		1942	1941	1942	1941*	1936-1940	1931-1935	1926-1930
New England	2,579,152	3	6	0.12	0.23	0.39	0.70	1.31
Middle Atlantic	13,129,185	20	31	0.15	0.24	0.43	0.80	1.40
South Atlantic	2,727,985	19	24	0.70	0.88	1.14	2.70	4.50
East North Central	9,386,378	13	19	0.14	0.20	0.53	0.75	1.29†
East South Central	1,286,747	7	9	0.54	0.70	2.54	4.81	8.31
West North Central	2,716,484	5	8	0.18	0.29	0.60	1.24	1.83
West South Central	2,048,692	15	28	0.73	1.37	3.09	5.36	7.32‡
Mountain & Pacific	4,186,039	13	16	0.31	0.38	0.60	0.88	1.80

† Data for South Bend for 1925-1929 are not available.
‡ Lacks data for Oklahoma City in 1926.
* 1940 census figures used.

The eleven cities (excluding Sacramento) in the Mountain and Pacific states (table 8) (population 4,186,039) report a decrease from sixteen deaths in 1941 to thirteen in 1942 (there were but thirteen deaths in 1940). The rate has decreased from 0.38 to 0.31. Sacramento has again been omitted in calculating the total number of deaths and the rates. This city reports no death. Seven of the Mountain and Pacific cities (Long Beach, Oakland, Portland, Sacramento, Salt Lake City, Seattle, Tacoma) report no death from typhoid in 1942. Long Beach, Oakland, Portland and Seattle have maintained their ranking of 1941. Portland and Seattle report no death during the past three years. It is stated that the one death in San Diego was among nonresidents. Of three deaths in Denver, one was among nonresidents. Los Angeles reports seven deaths, six among residents (there were ten in 1941, six among nonresidents). San Francisco records one death among residents (there were two in 1941, one among residents). With no death in 1940 and 1941, Spokane reports one among residents in 1942.

THE HONOR ROLL

The number of cities with no death from typhoid has increased from thirty-six to fifty. The three cities (Charlotte, Gary, Sacramento) not included in the ninety-three (table 11) also report no death. While this is by far the best showing, there remain four cities with rates of 2.0 or more. The charge of nonresident deaths accounts in part for these high rates. The number of cities with rates of less than 1.0 has increased by two (eighty-four in 1942, eighty-two in 1941). Thirty cities (thirty-one with Gary) record no typhoid death in 1941 and 1942 (table 9). There were only twenty-five cities a year ago that reported no death for a period of two years or longer. It is again emphasized that several other cities in the first rank would appear in the honor roll were they not charged with deaths among nonresidents.

For the seventy-eight cities (table 12) for which data are available since 1910 there occurred eighty-three deaths from typhoid, which is by far (less than one half that of 1940) the lowest of record. Deaths were recorded at the rate of 0.23 per hundred thousand of population. For the ninety-three cities the number of deaths in 1942 is ninety-five (141 in 1941). The rate has decreased from 0.50 in 1940 to 0.37 in 1941 and to 0.25 in 1942 (a 50 per cent reduction in two years). Of the ninety-five deaths in the ninety-three cities, thirty-two deaths (one third) were among nonresidents. The health officers report no special outbreaks of typhoid. Improvement has been general throughout the country but especially in the West South Central cities, where the highest rates have been reported during the past many years. War travel does not appear to have contributed to the typhoid problem in our large cities.

Council on Foods and Nutrition

ACCEPTED FOODS

THE FOLLOWING ADDITIONAL FOODS HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO ACCEPTED FOODS.

OFFICE OF THE COUNCIL.

PREPARATIONS USED IN THE FEEDING OF INFANTS (*See* Accepted Foods, 1939, p. 156).

Burroughs Wellcome and Company, Inc., New York.

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Calories.—4 per gram; 115 per ounce.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, AUGUST 21, 1943

PROBLEMS OF INFECTIOUS JAUNDICE

A full understanding of the disease or diseases called infectious or epidemic jaundice or hepatitis has not been reached, as the confusion of the nomenclature bears witness. Whether "catarrhal jaundice" in the old sense of jaundice ascribed by Virchow in 1864 and others before him [1] to closure of the common duct in the course of a duodenal "catarrh" occurs as a distinct disease is still questionable. Does the term possibly cover two morbid conditions, one due to biliary obstruction and the other to hepatic changes without obstruction? The present general view is indicated by the increasing use, particularly by European writers, of the term "infective or epidemic hepatitis." The nature of the hepatitis and of other changes has not been exhaustively studied, the mechanism of the jaundice has not yet been explained, and the cause or causes are not known; significant progress is being made, however, in the study of these problems.

By aspiration biopsy of the liver in 26 cases of sporadic jaundice of the catarrhal type Roholm and Iversen [2] confirmed previous reports of diffuse changes in the liver in such cases. A cannula was inserted in the posterior axillary line of the ninth right interspace through which were aspirated, by means of a record syringe, columns of liver tissue 1 to 2 cm. long and 2 mm. in diameter. The procedure was employed in various stages of the disease, but mainly one week or so after the appearance of jaundice and three or four weeks later. The liver presented a general disarrangement of its cells with necrobiotic changes, infiltration with mononuclear cells and increase of connective tissue in the portal spaces around the central veins and also in the lobules. Although pronounced in the first week, the changes subsided within a month after the appearance of the jaundice. The interlobular biliary ducts were normal. The jaundice may have been due to failure of the biliary pigment to reach the ducts on account of the changes in the liver cells. The occurrence of fatal subacute atrophy of the liver in one of the cases suggests again that fundamentally acute yellow atrophy may be of the same nature as the acute diffuse hepatitis. Findlay and Dunlop [3] found that in the literature "the association between epidemic catarrhal jaundice and acute necrosis of the liver has been extremely striking." The Danish investigators conclude that the diffuse hepatitis probably is hematogenous. Similar studies should be made in the course of epidemics of infectious jaundice and of jaundice following the injection of human plasma or serum.

Clinically this type of jaundice clearly concerns an infectious disease or diseases naturally communicable, mainly, so it seems, by contact, and produced artificially by the injection of human serum or plasma containing infectious icterogenic agents the exact nature of which is as yet unknown. Research may determine whether what is now termed infectious jaundice or hepatitis is a single disease and also settle the question whether the spontaneous and the artificial forms are identical. On request of the Ministry of Health, the Medical Research Council [4] in England has undertaken a comprehensive investigation of the incidence, causes and diagnosis of different forms of jaundice. This investigation is in competent hands, and valuable results will no doubt be forthcoming. Significant too is the growing concern about infectious jaundice, as shown by the fact that it has been made recently a reportable disease in Illinois and perhaps also in other states.

There are no specific diagnostic tests for infectious jaundice. In doubtful cases of fever with jaundice, leptospirosis (Weil's disease) or even yellow fever might be suspected. In leptospirosis the serum of the patient usually agglutinates Leptospira icterohemorrhagica, and the urine may transmit the infection to guinea pigs. In yellow fever microscopic examination of the liver will yield information of diagnostic value, and in recovered patients not previously inoculated against yellow fever search for protective bodies against the fever in the blood may be of help. In epidemics of infectious jaundice or hepatitis it is believed that the disease may be spread at least to some extent by patients whose symptoms suggest the disease but in whom jaundice does not appear. In such cases examination of the urine and the blood for biliary products may be of value.

Advances in the diagnostic, experimental and other aspects of infectious jaundice await the determination of its cause. In a previous editorial [5] reference was made to the transmission of the disease to volunteers

1. Klemperer, Paul; Killian, J. A., and Heyd, C. G.: The Pathology of "Icterus Catarrhalis," Arch. Path. **2**: 631 (Nov.) 1926.

2. Roholm, K., and Iversen, P.: Changes in the Liver in Acute Epidemic Hepatitis (Catarrhal Jaundice) Based on 38 Aspiration Biopsies, Acta path. et microbiol. Scandinav. **16**: 427, 1939.

3. Findlay, G. M., and Dunlop, J. L.: A Fatal Case of Acute Necrosis of the Liver Associated with Epidemic Catarrhal Jaundice, Brit. M. J. **1**: 652 (April 9) 1932.

4. Further Investigation of Hepatitis, editorial, Lancet **1**: 623 (May 15) 1943.

5. Catarrhal and Human Serum Jaundice, editorial, J. A. M. A. **122**: 746 (July 10) 1943.

by nasal washings in salt solution from patients with jaundice following the injection of yellow fever vaccine, and by the oral ingestion of duodenal washings as well as the injection of serum and blood from patients with spontaneous jaundice. Animal experiments with such materials do not seem thus far to have yielded any conclusively positive results. The failure to find any bacterial cause for infectious jaundice strengthens the suspicion current for some time that it may be a virus disease or diseases. A report[6] has come to the effect that a virus has been cultivated from the duodenal fluid of patients with "hepatitis epidemica" on the developing hen's egg. Further reports on work along this and other lines will be awaited with special interest.

HOUSING AND HEALTH

The exact effects of substandard housing on the health of the inhabitants are difficult to estimate; generally it is accepted that illness may be directly fostered by bad housing conditions. The concept of bad housing includes overcrowding; overcrowding alone facilitates the spread of certain infectious diseases, particularly tuberculosis, other contagious diseases of the respiratory system, and such diseases as diphtheria, scarlet fever and meningitis. Insanitary dwellings are usually overrun with rats, which also spread some diseases such as typhus. Insanitary conditions for disposal of excreta and improper central water supply, food and milk are more frequent in both urban and rural substandard housing areas. Typhoid and the dysenteries flourish in these regions. In some places mosquito breeding pools and unscreened dwellings are conducive to excessive malaria among the residents. The venereal diseases also are excessive in substandard and overcrowded housing regions. Diseases due to deficient vitamins or food and lack of sunshine are similarly frequent out of all proportion in areas where housing is deficient. The effect on the mental and emotional health of these residents, although more difficult to determine, must be considerable.

Improvement in housing is usually opposed by those who fear an adverse financial effect by removal of rental income and those who hesitate because of the cost. The medical profession is deeply interested in this as in all other factors which influence the health of the people. The elimination of bad housing along lines of sound practice together with the institution of suitable safeguards against the mere transfer of people from one area of bad housing to another is a program which the medical profession can urge as a contribution to the health of the community.

Such programs may be expected to improve the health records and general well being of the communities in which these steps can be taken. Good housing is not, however, a panacea for disease. Solution of the problem of substandard housing, for example, could not be expected to eradicate disease; it could not be expected to eliminate ignorance or poverty. It would not solve the problem of the supply and demand for medical care among the poor; it would not insure high standards of medical practice; nor would it furnish any guaranty that those removed from the slums—whether urban or rural—would become at once self-respecting, cleanly, hard working or economically successful citizens.

One of the most pressing health problems facing this country immediately after the end of the war will be the elimination of substandard housing conditions and the building of new facilities. The programs adopted to accomplish this end should be in process of planning now. In considering a housing program one must take into account its place in the general economic situation. If the cost of housing forces deficient nutrition, the housing may well be postponed. If transportation from a new housing area increases loss of time or absenteeism in work, it may not be a desirable benefit. If a housing project leads to racial warfare the result is not wholly a social gain. These considerations indicate again how many factors are involved in every move toward improved security and the necessity for taking every possibility into account in making final decisions.

BIOLOGIC PECULIARITIES OF INTRACRANIAL NEOPLASMS

Most intracranial tumors are characterized by several interesting biologic differences from tumors elsewhere in the body. Regardless of their rate of growth, degree of aggressiveness, ability to infiltrate and other characteristics usually associated with cancers, they do not metastasize to distant parts of the body. Cancers which arise elsewhere can metastasize freely into the central nervous system, indicating that the incompatibility of protoplasms is not absolute. When intracranial tumors metastasize they do so by implantation.

Using medulloblastomas as an example, Abbott and Kernohan[1] recently considered some additional special problems in the behavior of these tumors. They accept the statements that tumor cells are often free in the cerebrospinal fluid and that they spread by circulation of the fluid and by gravity. Such free cells from medulloblastoma, they point out, frequently become implanted, whereas in other tumors which are equally cellular they usually fail to grow. Thus this system appears to be unequally susceptible to the growth of neoplastic cells arising from the same system. Perhaps this problem is related to the general biologic problem of selective susceptibility and resistance of certain tissues to tumor growth such as is illustrated by the

6. Siede and Luz: Klin. Wchnschr., Jan. 23, 1943, quoted in Bull. Hyg. **18**: 361 (May) 1943.

1. Abbott, Kenneth H., and Kernohan, James W.: Medulloblastomas: Concerning the Problems of Spinal Metastases and Malignancy—A Report of Six Cases and Discussion of the Problems Involved, Bull. Los Angeles Neurol. Soc. **8**: 1 (March) 1943.

susceptibility of the spleen to the growth of malignant melanoma cells and its resistance to most other neoplastic cells.

The origin of medulloblastoma is believed to be from persistent fetal cells. Most of these tumors are found in childhood, but the time of beginning of their growth remains uncertain because the duration of the clinical course after the onset of symptoms shows wide variation. The implantation metastases may grow to large size and yet produce few symptoms. The authors consider the possibility that the multiple growths do not represent metastases but instead tumors of independent origin. As an explanation for the differences in behavior they suggest that the neoplasms now classified as medulloblastoma might really be several different kinds of tumors.

To the old unsolved problem of the failure to form distant metastases are added those of varying ability to metastasize locally by implantation, of multiple tumors versus metastases, of causes for the differences in rate of growth, and of the failure of many tumors to produce symptoms. Some of these problems may be solved by careful studies of the natural history of the tumors. For others fundamental chemical studies may be necessary.

Current Comment

SEMINAL FIBRINOLYSIN

Discovery of a proteolytic enzyme in human semen practically identical with the fibrinolysin secreted by virulent strains of hemolytic streptococci has been reported by Huggins [1] of the Department of Surgery, University of Chicago. Human, guinea pig and canine semens are delivered in a liquid state, after which human and guinea pig semens coagulate to form an elastic solid, while canine semen remains fluid. Coagulated guinea pig semen remains in a solid state in the vagina for several days. Solidified human semen is spontaneously liquefied in a few minutes. Seminal coagulation is believed to be due to fibrinogen and thromboplastin [2] derived from a special region of the prostate.[3] Liquefaction of the resulting coagulum is apparently due to the combined action of two enzymes, a fibrinolysin and a "fibrinogenase." "Fibrinogenase" is dominant in canine semen, thus preventing coagulation, while fibrinolysin is dominant in human semen, lysis taking place only after the formation of the seminal clot. This fibrinolysin is present in full titer in normal human prostatic secretion but is absent from hydrocele and spermatocele fluids and from all other human body fluids thus far tested. Many points of similarity occur between the human prostatic fibrinolysin and the streptofibrinolysin of Tillett and Garner.[4] Both liquefy normal human blood or plasma clot but are inactive against rabbit clots. Under certain pathologic conditions human blood becomes immune to streptolysin, presumably because of the presence of a specific antistreptococcus antibody. The same antibody neutralizes human seminal fibrinolysin. A theory is not as yet suggested as to the purposeful function of the newly discovered fibrin liquefying prostatic factor, which may well prove to be of practical clinical interest.

1. Huggins, Charles, and Neal, William: J. Exper. Med. **76:** 527 (Dec.) 1942.
2. Goldblatt, M. W.: Biochem. J. **29:** 1346 (June) 1935.
3. Walker, G.: Bull. Johns Hopkins Hosp. **21:** 182, 1910.
4. Tillett, W. S., and Garner, R. L.: J. Exper. Med. **58:** 485 (Oct.) 1933.

COURSE IN HEALTH EDUCATION

On page 1194 in this issue of THE JOURNAL appears an announcement of the lecture-observation-demonstration course in the health education and related work of the American Medical Association recently given to twenty-nine graduate students in health education studying under fellowships granted by the W. K. Kellogg Foundation and supervised by the United States Public Health Service. The visit of these students to the American Medical Association was arranged under authorization by the Board of Trustees [1] permitting the Bureau of Health Education to arrange such opportunities for qualified students. At the end of the week's work, officers of the United States Public Health Service who accompanied the group and members of the group expressed amazement at the scope and character of the work of the several departments of the American Medical Association, of which they had previously had only the vaguest idea. It was the consensus of the group and of the headquarters staff who participated in the demonstrations that the benefits of such a visit are mutual. The students learn much about the medical profession, and the medical profession in turn will benefit by better understanding and cooperation on the part of these students when they make their contacts with physicians in their life work as health educators attached to local (city and county) health departments.

DRUGS AND ESSENTIAL HYPERTENSION

THE JOURNAL [1] recently commented on the extreme fluctuations of the blood pressure which may occur without drug intervention. J. S. Kapernick [2] has reported a study of several drugs which permitted him to conclude that these drugs, "when administered continuously in optimal dosage for periods of four weeks, do not possess any significant hypotensive effect on the blood pressure of hypertensive patients." The agents used in the study were those which are in current use and which are claimed to be of value in the management of essential hypertension. The study was thorough and the results are of practical clinical value. The value is emphasized in a discussion of the presentation by E. A. Hines, who stated in part: "In a review of the many articles in the medical literature concerned with the treatment of hypertension it will be observed that

1. Abstract of Minutes of Meetings of Board of Trustees Held Feb. 18-20, 1942, J. A. M. A. **118:** 906 (March 14) 1942.
1. Fluctuations in Hypertension, Current Comment, J. A. M. A. **121:** 519 (Feb. 13) 1943.
2. Kapernick, J. S.: The Blood Pressure in Essential Hypertension: Effect of Several Reputedly Hypotensive Drugs, Proc. Staff Meet., Mayo Clin. **18:** 187 (June 16) 1943

in general the results obtained are in inverse proportion to the care with which the study was carried out; in other words, the more adequately controlled the study, the less likely are the results to have been favorable. It is not probable that the false conclusions which were drawn from these studies were the result of wilful misrepresentation or misinterpretation or even of wishful thinking. What then accounts for such a state of affairs? Essentially the confusion is due to attempts to devise a cure without adequately studying the fundamental nature of the disease. More specifically, the false conclusions are due to two things which Dr. Kapernick has largely avoided in this study: (1) the tendency to consider symptomatic relief as the chief criterion of the effectiveness of a drug in the treatment of hypertension and (2) the failure to recognize the importance of the inherent variability of the blood pressure in estimating the effects of various drugs on the blood pressure. This is not to say that symptomatic relief is not desirable in treating hypertensive disease, but it has become apparent that the symptoms associated with hypertension are seldom directly related to the actual height of the blood pressure nor is symptomatic relief necessarily related to survival."

COLLATERAL IMMUNITY IN TUBERCULOSIS

Experimental evidence in support of the belief that an active tuberculous nodule is associated with an increased resistance to numerous other infectious diseases has been recently reported by Ascoli [1] of Middlesex Veterinary School, Waltham, Mass. Twelve years ago it was demonstrated by Bareggi [2] and other Italian investigators that calves previously vaccinated subcutaneously (not intravenously) with BCG recovered from Pasteurella vituliseptica infections which proved fatal to nonvaccinated control calves and that guinea pigs with subcutaneous tuberculous nodules are insusceptible to experimental foot and mouth disease [3] and to Brucella abortus infections.[4] Extirpation of the tuberculous nodules in these guinea pigs was followed by a loss of the nonspecific acquired resistance. Transplantation of the extirpated nodule into normal guinea pigs increased their collateral nonspecific resistance immediately without the delay which occurs following routine methods of vaccination.[5] The role of a local tuberculous nodule to increase nonspecific resistance has been amply confirmed on calves.[1] Thus far no acceptable theory has been proposed to account for this collateral panimmunity. It is conceivable that the local tuberculous nodule gives off nonspecific hormones or other growth promoting chemical products, which activate or stimulate nonspecific cytologic defenses in other parts of the body. According to Brown and Pearce [6] a similar "anachoretic" panimmunity is caused by a local syphilitic lesion. Ascoli believes that the "anachoretic" phenomenon is also shown by numerous other local proliferative or inflammatory tissues. If so, his "anachoretic" collateral panimmunity would be of wide clinical application.

1. Ascoli, Alberto: J. Immunol. **45**: 141 (Oct.) 1942.
2. Bareggi, G.: Biochim. e terap. sper. **17**: 161 (April 30) 1930.
3. Vaghi, L.: Biochim. e terap. sper. **17**: 295 (July 31) 1930.
4. Ascoli, Alberto; Bassi, A., and Massironi, G.: Pat. compar. d. tuberc. **4**, No. 2, 1938.
5. Ascoli, Alberto: Proc. 3d Internat. Cong. Microbiology, 1940, p. 622.

MARKLE FOUNDATION SUPPORTS STUDY IN TROPICAL MEDICINE

The usual activities of the John and Mary R. Markle Foundation consist of grants in aid of specific research projects in the field of medical sciences. This policy has remained unchanged by the war. The foundation in 1942 was particularly helpful to work in tropical medicine.[1] The first grant in this field was an appropriation of $40,000 to the National Research Council to establish a number of lectureships in tropical medicine in medical schools. The foundation also appropriatel $25,000 to the Association of American Medical Colleges to finance the emergency training of teachers of tropical medicine. Under this arrangement each medical school in the United States and Canada which did not have on its staff at least two men qualified to teach tropical medicine was invited to send a member of its teaching staff for a two months course in tropical medicine at the Army Medical School in Washington and another member of its staff to the Department of Tropical Medicine at Tulane University for a similar course. Aid has also been given to collecting laboratory specimens and slide materials to assist in the teaching of tropical medicine in medical schools. Other grants of the foundation in 1942 covered a wide range of medical subjects including the fields of infections and immunity, ophthalmology, nutrition, chemotherapy, pharmacology, anatomy and physiology, neurology and psychiatry, biochemistry and blood and the cardiovascular system.

THE POLIOMYELITIS SITUATION

The incidence of poliomyelitis in some parts of the United States has reached almost epidemic proportions. Indications are that this will be the worst year for this disease since 1940, when 9,770 cases were recorded. Through August 7 nearly 3,000 cases have been reported, or more than twice as many as appeared during the similar period last year. Elsewhere (p. 1198) appears a tabulation of the latest available figures of reported cases for the areas where this disease is particularly excessive. California, Texas, Oklahoma and Connecticut appear to be the states that are the most seriously affected. Most other parts of the country are relatively unaffected, with no more cases of poliomyelitis than would be expected at this time of year.

6. Brown, W. H., and Pearce, Louise: The Resistance (or Immunity) Developed by the Reaction to Syphilitic Infection, Arch. Dermat. & Syph. **2**: 675 (Dec.) 1920.
1. The John and Mary R. Markle Foundation, Annual Rpeort, 1942, 14 Wall Street, New York.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war, and such other information and announcements as will be useful to the medical profession.

PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS, DENTISTS AND VETERINARIANS

THE COMMISSIONING OF INTERNS AND RESIDENTS

The Officer Procurement Service, Washington, D. C., issued a memorandum (FT-108) on August 7 to commanding generals of service commands, explaining the action to be taken in procuring physician interns and residents for appointment in the Medical Corps of the Army and requiring immediate action by each district office. The physicians to whom this memorandum applies are (1) interns graduated from medical schools during March-June 1943 who have not yet been commissioned in the Army and Navy and (2) residents who graduated in June 1942 or before who have not yet been commissioned in the Army and Navy. All such interns and residents are eligible for commissioning except those previously physically disqualified by the Surgeon General or otherwise ineligible for commissions under army regulations. Interns and residents qualified by Selective Service as IV-F because of physical disability and female interns and residents are potential candidates.

The source of such candidates for medical commissions are the public and private hospitals with 50 or more beds. Immediate contact with the superintendent of all such hospitals must be made requesting the names of all potential intern and resident candidates and permission to get in touch with them at times convenient to all.

District offices will use every effort to sell potential candidates on their patriotic duty to take steps to qualify for commissions. Deferment from induction will not be available to potential candidates on completion of their current internships and residencies. No such candidate who is commissioned will be called to active duty until the completion of his internship or residency. The Army has no intention to deprive hospitals of the services of necessary physicians, interns and residents until completion of their internships and residencies; it has every intention, the memorandum states, to commission in the Medical Corps all such interns and residents at the earliest possible moment, postponing their call to active duty until the completion of their respective terms of their internships and residencies. A list of the names of all potential candidates in these groups who refuse or wilfully neglect to be processed for commission will be maintained.

All potential candidates covered by this memorandum are deemed to be "cleared" by the Procurement and Assignment Service and to have been "determined as available," in accordance with a letter from the Procurement and Assignment Service dated August 7 addressed to all superintendents of hospitals having interns and residents and to corps area and state chairmen. On the same day on which the interns and residents fill out their applications, the hospitals which these physicians are serving should apply to the state chairman of the Procurement and Assignment Service for their deferment until the terms of their internships and residencies have expired. All interns are deferred for the term of one year internship, but if a resident is deemed by the Procurement and Assignment Service as not essential to the hospital he should accept a commission and expect to go on active duty immediately.

THE NAVY WANTS SIX HUNDRED WOMEN DOCTORS

Reserve commissions in the Medical Corps of the Navy are now open to qualified women physicians in the ranks of lieutenant commander, lieutenant and lieutenant (junior grade). The Bureau of Medicine and Surgery has announced an initial request for six hundred women doctors, two hundred of them to be commissioned in each of the available ranks.

Under the terms of Public Law 38, passed by Congress last spring, women doctors are being accepted in the Medical Corps with the same status as men doctors. They will be assigned to duty at various types of shore medical establishments within the continental limits of the United States.

In applying for commissions in the Medical Corps, women doctors must meet the same professional requirements as men and must be approved for military duty by the Procurement and Assignment Service for Physicians in order to prevent undue depletion of medical services in civilian communities. The policy has also been established that women doctors will not be accepted if they are married to Navy men or if they have children under 18 years of age.

The general requirements for women physicians are these: For general medical officers the age limits are 21 to 35; for specialist medical officers the age limits are 27 to 50. Applicants must be graduates of an accredited medical school and have had at least one year's internship in an approved hospital. They must be duly licensed to practice medicine and be a member of a state or local medical society.

An exception to these requirements is made for women who apply for commissions as general medical officers immediately on completion of medical school. In this case the internship, license and membership stipulations may be waived.

In addition, applicants for specialist commissions must have had at least three years' recent practical experience in a particular specialty.

The eight women doctors at present holding commissions as lieutenants (junior grade) with the W-V(S) classification of the Women's Reserve, U. S. Naval Reserve, are eligible for transfer to the Medical Corps with an MC-V(S) or MC-V(G) classification.

Applications should be submitted to the nearest office of Naval Officer Procurement.

APPOINTMENT OF OFFICERS FROM CIVIL LIFE

The Acting Secretary of War, Robert P. Patterson, on July 13 issued a memorandum to the Secretary of War's Personnel Board, Officer Procurement Service, commanding generals of the Army Ground Forces, the Army Service Forces and the Army Air Forces, and Divisions of War Department General Staff, pointing out that, during the period of very rapid expansion of the Army last year and of the critical shortage of commissioned officers, civilians were appointed in larger numbers to commissioned grades. Now the Army is rapidly approaching

its maximum planned strength and officer shortages, except in certain very critical categories, namely officers of the medical department, service pilots and chaplains, have been largely overcome. The Acting Secretary of War, therefore, directed that hereafter the Secretary of War's Personnel Board closely scrutinize all recommendations for appointment of civilians other than the exceptions noted and withhold approval in all cases in which it is not clearly indicated that the individual concerned possesses outstanding special qualifications of a technical or professional nature urgently required by the army and not obtainable from any other source; also that more effective methods be adopted, under direction of the General Staff, to classify properly and assign personnel now in the service, to the end that requirements for commissioned officers with professional or technical qualifications other than those indicated be obtained through the reassignment of qualified officers or through the selection and appointment of qualified enlisted men, that the Assistant Chief of Staff take action to reduce to the minimum the number of special categories that may be appointed from civil life and that the commanding generals of the three major commands and their subordinates refrain from requesting the appointment of civilians as commissioned officers except in cases in which the need is so urgent and the qualifications of the individual so unusual that no other solution is possible.

ARMY

HOSPITALIZATION IN THE FINAL BATTLE IN TUNISIA

Lieut. Gen. Omar Bradley, commander of the U. S. Army Second Corps in the final battle in Tunisia, in his report to Gen. George C. Marshall, chief of staff, covering operations between April 23 and May 9, made the following comments concerning hospitalization:

"The medical plan was drawn up so as to provide quick evacuation. Initial locations placed the evacuation hospitals within sound of artillery fire and almost within sight of some of the enemy's bombing operations. Locating these units well forward, however, in no way affected the efficiency of the doctors and nurses, who displayed an admirable coolness and accomplished results which, under normal hospital conditions, would have been considered excellent. Their forward locations reduced the time interval necessary for a wounded man to receive adequate care.

"The ambulance hauls to the base hospital at Bone varied from 85 to 110 miles over rough and tortuous roads. This distance was too great for evacuation of seriously wounded patients, particularly chest and abdominal cases. As a result the evacuation hospital which had initially been set up to take care of patients who would remain in the area until they could return to duty was given the mission of attending to the more seriously wounded.

"When the enemy surrendered in northern Tunisia he was operating a total of five hospitals, a total of 600 beds. By May 12 there were 745 enemy patients in our hospitals.

"Blood donors in the hospitals became a problem, and additional personnel from depot companies and clearing companies of medical battalions were utilized for this purpose. One hospital unit formed its own blood bank by cross matching these individuals, withdrawing the blood and placing it in refrigerators where it was easily accessible. It was found that this blood could be kept for several days and then given cold."

SITES FOR MORE ARMY HOSPITALS

Brig. Gen. Joseph B. Sweet, commanding general of the Communications Zone, is reported to have announced that a site has been selected near Beaumont, Calif., for an army hospital of about 750 beds, which it is expected will be completed in October. According to the Banning, Calif., *Record* of July 22, another army hospital of 1,000 beds is to be constructed at the city limits of Banning. An evacuation hospital has already been established on this site to take care of soldiers from the desert area.

PRISONERS OF THE JAPANESE

According to the Pratt, Kan., *Tribune* of May 21, Capt. William E. Wilson of the U. S. Army Medical Corps is being held prisoner of the Japanese in the Philippine Islands. Captain Wilson graduated from the University of Colorado School of Medicine in 1928 and entered military service on Dec. 12, 1940.

Dr. Nelson Kauffman, formerly of Indianapolis and recently with the thirty-first infantry of the U. S. Army, which was stationed in the Philippines, is reported to be a prisoner of the Japanese in a Yokahama prison camp.

CAPTAIN SANDERSON—MEDAL FOR BRAVERY

According to the La Porte, Ind., *Herald Argus* of June 17, Capt. Richard J. Sanderson, formerly practicing physician in Westville and Wanatah, Ind., has been awarded a medal for bravery beyond the call of duty while serving as a flight surgeon with a bomber squadron in New Guinea. Captain Sanderson was assigned to a bomber squadron at Shreveport, La., and later went to Greenville, N. C., and Ann Arbor, Mich.; in midsummer 1942 the squadron left San Francisco for Hawaii, Australia and New Guinea. Captain Sanderson's heroic deed was recently described as follows in the Chicago *Daily News*:

"Somewhere in New Guinea: Today the soldier's medal was awarded to Capt. Richard J. Sanderson of Westville, Ind. The night after Christmas a B-24, taking off from a darkened runway, cracked up and fell burning in the trees, carrying a full load of 500 pound bombs. As the wreckage burned, with explosion imminent, Sanderson crawled forward to try to save Sgt. Chalmers Yielding of Birmingham, La., who had been thrown out. He reached Yielding and began dragging him back as the wreck exploded. Both escaped, but Yielding later succumbed."

Captain Sanderson graduated from the University of Cincinnati College of Medicine in 1936.

TWENTIETH CLASS OF MEDICAL ADMINISTRATIVE CORPS OFFICERS

The twentieth class of Medical Administrative Corps Officers at the Officer Candidate School, Camp Barkeley, Texas, graduated on July 21 as second lieutenants. The graduating class, comprising two companies, will report to their new stations after ten day leaves and will assume the duties of supply, personnel, training and evacuation in the Army Medical Department. Brig. Gen. Roy C. Heflebower, commandant of the school, delivered the graduating address and presented the new officers their letters of commission and their diplomas. Col. George E. Armstrong, assistant commandant, directed the ceremonies and Major Miles G. Bell, executive officer, administered the oath of office.

BURIAL EXPENSES OF MILITARY PERSONNEL

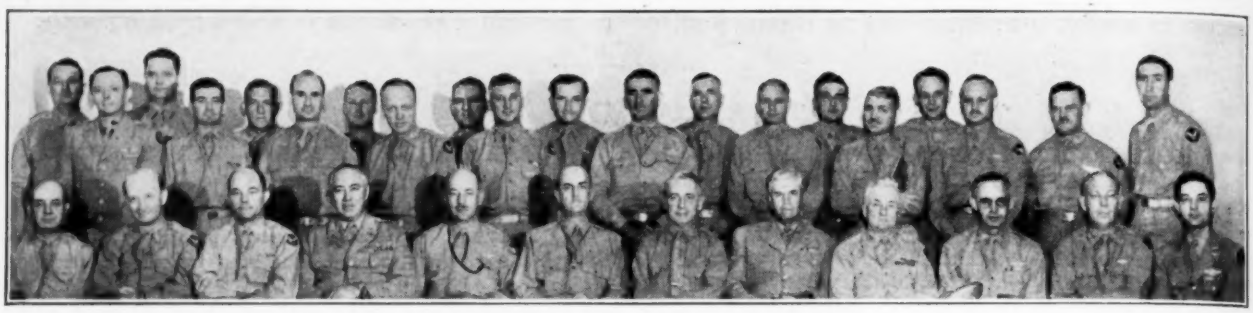
Headquarters of the Sixth Service Command, Chicago, issued instructions on August 3 to commanding officers of all camps and posts in that service command calling attention to War Department Circular No. 149, dated June 30, which prescribes that burial expenses of military personnel of the United Nations who may die in continental United States are payable from the regular army appropriation. The Sixth Service Command directed that, in each case in which expenses of disposition of remains of such personnel are paid, a certified copy of the invoice to be used in the substantiation of settlement or a certified copy of the purchase order in lieu of the invoice be furnished.

CONFERENCE ON AVIATION MEDICINE

Rapid strides made by aviation medicine, both in research and in practice, were discussed by the senior surgeons of all commands and the four continental air forces at a three day meeting at Army Air Forces headquarters in Washington, D. C. The meeting was called by Brig. Gen. David N. W. Grant, Air Surgeon.

Those who attended are, front row, left to right, Col. Wood S. Woolford, chief of operations, Air Surgeon's Office; Col. Charles R. Glenn, surgeon, Training Command; Col. Robert K. Simpson, surgeon, Gulf Coast Training Center; Col. Cadmus J. Baker, surgeon, First Air Force; Brig. Gen. Eugen G. Reinartz, commandant, School of Aviation Medicine; Brigadier General Grant; Col. Fabian L. Pratt, surgeon, Fourth Air Force; Col. Ernest F. Harrison, surgeon, Matériel Command; Col. Irwin B. March, surgeon, Eastern Technical Training Command; Col. Duran H. Summers, surgeon, Antisubmarine Command; Col. Henry C. Chennault, chief of profession services, and Col. William H. Powell Jr., surgeon, Atlantic City, N. J.

Those in the back row, left to right, are Col. Dan C. Ogle, surgeon, Army Air Forces Regional Station, Coral Gables, Fla.; Col. Mel Pazdral, surgeon, Southeastern Training Command; Lieut. Col. Howard A. Rusk, professional division, Air Surgeon's Office; Col. Wilfred F. Hall, surgeon, Miami Training Center; Col. Clyde L. Brothers, surgeon, Third Air Force; Col. E. L. Gann, chief of personnel section, Air Surgeon's Office; Col. Harold H. Twitchell, surgeon, Second Air Force; Col. Walter S. Jensen, executive officer, Air Surgeon's Office; Major Hugh Mullan, Air Service Command; Col. Robert M. Allott, surgeon, Sioux Falls Army Air Base Station Hospital; Col. William F. De Witt, surgeon, Station Hospital; Col. Michael G. Healy, surgeon, West Coast Flying Training Command; Lieut. Col. Austin Lowrey Jr., surgeon, Proving Ground Command; Col. Otis B. Schreuder, surgeon, Air Forces School of Applied Tactics; Col. William P. Holbrook, chief of professional placement branch, Air Surgeon's Office; Col. Gustave E. Ledfors, chief of supply, Air Surgeon's Office; Col. Ehrling L. Bergquits, surgeon, Technical Training Command; Lieut. Col. Sheldon S. Brownton, surgeon, Training Command; Col. Paul W. Gilliland, surgeon, Air Transport Command; Col. Loyd Eugene Griffis, chief of research division, Air Surgeon's Office.



Those who attended the conference on aviation medicine.

NAVY

THE WAVES DO EXCELLENT WORK

The Bureau of Medicine and Surgery has received many favorable comments concerning the excellent work being done by the Hospital Corps Waves on duty at naval hospitals throughout the country. Among the 600 selected monthly, more than 10 per cent are qualified technicians in the allied fields of medical work, about 10 per cent are college graduates, and about 25 per cent have one year or more years of college. The Waves being accepted for the Hospital Corps of the Navy are a true cross section of young womanhood in America and represent rural communities, large cities, factories, farms and schools. Their work is vitally important in that it releases male hospital corpsmen for sea or foreign service.

ADDITIONAL FACILITIES FOR CONVALESCENTS

The assistant chief of the Bureau of Medicine and Surgery, Rear Admiral Luther Sheldon Jr. (MC), U.S.N., it was announced on August 9, will inspect naval convalescent hospital facilities and equipment in the eighth, eleventh, twelfth and thirteenth naval districts and will examine various sites for their possible use as additional convalescent hospital expansion. Commander Francis I. Braceland (MC), U.S.N.R., of the neuropsychiatry section, division of physical qualifications and records, who will accompany Admiral Sheldon, will examine the facilities available for navy neurologic cases in the inspection area.

CLASS IN DEEP DIVING

The Bureau of Medicine and Surgery announces that a class in deep diving for medical officers will be assembled at the Diving School, Navy Yard, Washington, D. C., on September 13, and that twelve medical officers have been assigned to this instruction.

LIEUTENANT McCAMPBELL CITED

The commander of the South Pacific Area and South Pacific Force has commended Lieut. (jg) Bruce R. McCampbell, MC, U.S.N., for service set forth in the following citation: "For skilful and effective performance of duty while serving on board a destroyer which participated in the engagement with Japanese forces off Guadalcanal, British Solomon Islands, on Aug. 7, 1942. As medical officer of the vessel he rendered skilful aid to members of the crew who were wounded by enemy bombs. When his ship picked up four hundred survivors, more than half of them were in need of medical aid. By untiring efforts he rendered emergency treatment to two hundred and fifty persons in forty-five hours. His zealous conduct was in keeping with the highest traditions of the Naval Service."

Lieutenant McCampbell graduated from the University of Tennessee College of Medicine in 1941, was a student intern for two years at the U. S. Marine Hospital in Memphis, Tenn., and was an intern at the Naval Hospital, San Diego, Calif. He was promoted to the rank of lieutenant in March 1943.

PRISONERS OF THE JAPANESE

Lieut. Mack L. Gottlieb, MC, U.S.N., formerly of New York, was captured by the Japanese while serving at the naval hospital in Guam and is now a prisoner of war at Zentsuji War Prison Camp at Shikoku, Japan. Dr. Gottlieb graduated from New York University College of Medicine in 1930, is a member of the American College of Physicians and the American Medical Association, and has been granted a certificate by the American Board of Internal Medicine.

According to *Northwest Medicine*, Lieut. Comdr. Clyde L. Welsh of Seattle, reported missing since July 1942, is declared a prisoner of the Japanese, probably in the Philippines. When action began in the Philippines he was stationed at Canacao Hospital, near Cavite.

MISCELLANEOUS

RECOMMENDED STANDARD FOR HOSPITAL SHEETING

The National Bureau of Standards, Washington, D. C., has circulated to the industry for written acceptance a recommended commercial standard for hospital sheeting for mattress protection (nonrubber), TS-3551, adopted at a meeting of a committee representing the American Hospital Association with a committee of manufacturers. This recommended commercial standard is being circulated to producers, distributors and users of hospital sheeting for written acceptance as a basis for publication by the National Bureau of Standards. This recommended commercial standard as adopted by the committee goes into such general requirements as fabric, material and workmanship, resistance to mineral oil, resistance to disinfectants and sterilization, water permeability, resistance to cracking, burning rate, thickness, width and length and tearing strength and also briefly outlines the methods of testing for these requirements.

CINCHONA BARK IMPORTS RISE SHARPLY

According to the Office of the Coordinator of Inter-American Affairs, expansion of cinchona bark production in South and Central America is helping replace the loss of quinine supplies in the Far East. Cinchona bark production from Latin America is increasing steadily. In June cinchona imports from the other Americas were more than twice the average of the previous five months.

Development projects include preparation for distributing 3,000,000 cinchona seedlings from the El Porvenir plantation in Guatemala, the largest in the Western Hemisphere. This is part of the program to supplement collection of bark from wild trees. The large June imports of cinchona came from Bolivia, Peru, Ecuador and Colombia and from other scattered sources. The El Porvenir plantation, with about 1,000 acres of cinchona, could supply a substantial portion of the entire United States quinine needs for a considerable period if all the trees were cut down. A number of trees are being weeded out under scientific forestry methods. The bark of these trees will be shipped immediately. Meanwhile the 300,000,000 seeds will be put in beds. Seedlings will be set out in Guatemala.

Use is being made of 2,000,000 cinchona seeds brought out of the Philippines by Col. Arthur F. Fischer. Of these, 200,000 have been planted and have developed into seedlings at the Beltsville, Md., station of the U. S. Department of Agriculture. It is planned to put the rest into seed beds and then into nurseries in Costa Rica.

In Peru, bark from the wild trees is being collected on a large scale, and work is progressing on a plantation near Tingo Maria, Peru, east of the Andes. The United States is aiding this plantation with financial and technical aid.

MEDICAL SUPPLIES ON U. S. SHIPS

Ships sailing under the control of the War Shipping Administration which do not have ship's doctors aboard henceforth will be stocked with a revised minimum standard supply of drugs and medical supplies prescribed by the United States Public Health Service, it was announced on August 7. The revised edition of "Ship's Medicine Chest and First Aid at Sea," published by the United States Public Health Service, lists ninety-nine standard articles and how to use them. The list includes a variety of recognized medical supplies. Forty-six of the prescribed items, such as phenobarbital, sulfanilamide and sulfathiazole, are listed as "drugs." Although War Shipping Administration operated ships almost always travel in convoy, which always affords doctors, the administration is now in the midst of a training program which will eventually provide pharmacist's mates aboard all merchant ships. In addition, all officers are required to pass an extensive first aid course. The administration states that the items it listed as standard were considered minimum for the protection of the crew. Agents will be permitted to add additional items which they consider advisable.

PUBLIC HEALTH UNDER HITLER

According to NPD, Germany, June 1, a new typhus institute under the direction of Prof. Dr. Hoffmann and equipped with the most modern appliances has been opened in Berlin.

It is reported from the commune of Garany, Zemplen County, according to *Reggeli Magyarorszag*, Hungary, of April 21 that plague has broken out among the half year old pigs which have not yet been inoculated.

NPD, Germany, June 5, reports that during the past year seven new children's hospitals have been established in East Prussia alone; besides these, six new nurses' training schools have been opened.

NPD of May 29 reports from Minsk that the German civil administration of White Ruthenia announces that a medical university (Hochschule für Medizin) will be founded in Moghilev for the training of medical students there. To begin with, German professors will be at the head of this university. The medical installations for the institute have already arrived from Germany.

According to *Hrvatski Narod*, April 29, last year 1,101,037 inspections and 317,436 detailed examinations were carried out in Croatia. Spotted typhus was proved in 10,509 cases, 712 of which proved fatal; stomach typhus in 5,099 cases with 453 deaths. Eighteen new health centers, organized to combat this disease, disinfected 231,134 persons as well as 134,266 railway carriages. Quarantine institutions were organized in Besanski-Brod, Sisak and Dugoselo, and twenty-two provisional hospitals have been erected for infectious diseases. The cost of these undertakings amounted to 143 million kune, of which 35 was spent on personnel and 108 on materials.

NDZ, June 25, reports that the health of expectant mothers may be endangered if, because of the great distance of their home from their work, they have to use means of transport which involve a great deal of vibration. In such cases the reich minister of labor has decreed that an inquiry be made whether the expectant mother should not be directed to a suitable job at a more favorably situated place of work. The inquiry will be carried out by the Labor Office, which will arrange a transfer if the circumstances warrant it. In order that the expectant mother's first job may be kept for her she may be given leave of absence for the period of her transfer.

DNB, June 28, reports that the reich minister of labor has directed that expectant mothers and women in childbed who have lost their job through the closing down of the establishment or through enemy action are to be granted the increased confinement benefits (confinement allowance, nursing allowance and so on) in accordance with the Law for the Protection of Mothers if they could have claimed confinement benefit had the job not come to an end. The amount of the confinement allowance depends on the amount of the last wages earned by the expectant mother. The order was to come into force on July 1. The increased benefits will be granted retrospectively from the beginning of the period for which the expectant mother can claim benefit.

Brusseler Zeitung, June 5, in its report of Reeder's speech, reproduces the following statement on the general health situation of the Belgian population: "England, who cuts off Belgium from her food supplies, feels obliged to complain about the bad state of health, the increased tuberculosis among Belgian children and adults, and that at a time when explosive toys are being dropped from British airplanes on Germany and Italy. . . . All possible care and precautions are taken against diseases migrating westward, such as scarlet fever and diphtheria. On January 1 it was stated that tuberculosis is only 10 per cent higher than it was before the war. This increase is easily attributable to war circumstances."

The *Neues Wiener Tagblatt*, June 24, states that according to the Vienna *Rathausnachrichten* the number of cases of scarlet fever has recently considerably increased in Vienna as in the rest of Europe. In order to ward off this danger, Stadtrat Professor Gundel of the central health office of Vienna has ordered the closing of all volksschulen, hauptschulen, hilfsschulen and hohere schulen. All children between the ages of 2 and 18 will be vaccinated against fever and diphtheria.

ORGANIZATION SECTION

OFFICIAL NOTES

LECTURE-OBSERVATION-DEMONSTRATION COURSE IN HEALTH EDUCATION

From August 2 through August 6 twenty-nine graduate students under fellowships from the W. K. Kellogg Foundation and the supervision of the United States Public Health Service spent a week of observation, study and demonstration of the health education and related work of the American Medical Association at the Association headquarters building in Chicago.

The following features were covered in the program:

Monday, August 2. Announcement of week's plans; division into groups; distribution of reference packets; history of the American Medical Association; organization and work of the American Medical Association; tour of the Association building; health education in industry.

Tuesday, August 3. Radio and health education, including demonstrations by transcription of radio interviews and dramatizations; tour of NBC and Blue Network studios.

Wednesday, August 4. The work of the following departments of the American Medical Association, presented in each instance by its director: Bureau of Investigation; Council on Pharmacy and Chemistry; Press Relations and Medical News; *Hygeia*, the Health Magazine; *Hygeia* reprints and pamphlet publications; health meetings and speakers.

Thursday, August 5. Journal publications and library services of the American Medical Association; group demonstrations of the organization and work of the Bureau of Health Education; guided tour of Chicago Museum of Science and Industry.

Friday, August 6. Traveling exhibits for the public; scientific exhibits; motion pictures; answering health questions by correspondence; summary and conferences.

Each student was furnished with an extensive collection of reference materials and each was given opportunity for personal consultation with the head of that Association department whose work most interested the student.

MEDICAL ECONOMIC ABSTRACTS

THE HEALTH PROGRAM OF THE U. S. BUREAU OF CENSUS

The United States Bureau of Census is located in a Maryland suburb 6 miles from Capitol Hill, Washington, D. C. Owing to the fact that the census is collected only every ten years, there is a great fluctuation in employment. During the census period there may be as high as 10,000 employees, but at present only 700 are classified as permanent. Eighty per cent are females and about 65 per cent white persons.

On Sept. 1, 1942 Dr. Leon Schwartz of the United States Public Health Service was assigned to the Bureau of Census to organize and conduct a health program. The program involves accurate absenteeism records, checked not only by the medical staff but by home visiting of all ill employees; for the preventive side the medical officer is readily available for medical advice; a program on medical education is conducted, necessary inoculations are given and sanitation of all work places is to be maintained at a high standard.

A laboratory and technical service will provide a minimum diagnostic service, the results of which will be made available for the use of the employees' private physician. Disability occurring during the work day will usually be treated within the emergency room with opportunities for rest available. Disabilities outside the building are generally referred for treatment to an outside physician. Because of the isolated location of the building it is probable that some therapy will be given at the place of employment. Office hours will be for consultation from 9 a. m. to 5:30 p. m. daily except Sundays.

CARE OF MEDICALLY INDIGENT IN NEW YORK CITY

A report of the Committee on Medical Economics of the Medical Society of the County of New York, adopted by the Comitia Minora, offers a plan for the care of the medically indigent containing some new features.[1] A nonprofit agency is to be set up with the membership of the board of directors divided equally among city officials, physicians of the five county medical societies of Greater New York and prominent citizens acceptable to the first two classes represented. Physicians are to receive $2 per house visit and $1 per office visit. A central municipal registration bureau is to be established and the city districted with a medical panel for each district to which all licensed doctors of medicine are eligible. Arrangements are made for a specialist's care. Diagnostic tests are to be provided in clinics without charge.

Medical indigence is defined to include single persons who have an annual income of $1,000 or less, $1,450 for man and wife and $250 for each dependent, not to exceed $1,950 per family.

The chief executive is to be a paid physician.

Panel calls except for emergency are to be received between 8 a. m. and 8 p. m. Patients treated after those hours will be charged an additional fee.

1. Recommendations for the Care of the Medically Indigent, Science **98**: 56 (July 16) 1943.

WOMAN'S AUXILIARY

California

For some time women of the Los Angeles County Medical Auxiliary have been coming together to do Red Cross work. Now they have their own Red Cross unit. Another project of this auxiliary was the furnishing of four day rooms at Camp Santa Anita. Dr. William R. Molony Sr., president of the California Medical Association, and Mr. Manuel Aguilar were guests of honor at the January meeting.

The San Benito County auxiliary, with a membership of only 6, sponsored a dancing party in San Juan which netted them $495.60. This money was used to furnish a room in the Hazel Hawkins Hospital, Hollister, to be used by the Red Cross.

Oklahoma

The Oklahoma County medical auxiliary met in the Venetian Room of the Y. W. C. A. in Oklahoma City and sewed on layettes, which were placed at the disposal of the city hospitals. The special project of the auxiliary this year is the meeting of troop trains and serving the boys gum, candy and cigarets. Of 32 members interviewed, it was found that they have averaged more than one hundred hours each in war service. Mrs. R. O. Early tops the list with eight hundred hours.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Licenses Revoked.—The California State Board of Medical Examiners at its meeting in San Francisco, June 28-July 1, revoked the licenses to practice medicine of Drs. Lillie L. Koerber and William E. Glaeser, both of San Francisco, for allegedly performing illegal abortions.

Nasopharyngeal Cultures Discontinued.—Nasopharyngeal cultures as a routine procedure before the discharge of a meningococcic meningitis patient have been abandoned at the San Francisco Hospital following a study in which it was observed that of 88 nasopharyngeal cultures on 44 patients since January 1 no positive cultures had been reported to June 7. An announcement stated that, as nearly all the patients have been given sulfonamide therapy, the question arises that perhaps the use of sulfonamides precludes the possibility of a convalescent carrier state.

Professor Ogden Goes to Texas.—Dr. Eric Ogden, associate professor of physiology at the University of California Medical School, Berkeley, has been appointed professor of physiology at the University of Texas Medical Branch, Galveston, and clinical physiologist at the John Sealy Hospital. A native of England, Dr. Ogden, who is a member of the Royal College of Surgeons and a licentiate of the Royal College of Physicians, graduated at the University College Medical School, London, where he was Sharpey Scholar and later a demonstrator in physiology. He joined the California faculty as instructor in physiology in 1929.

Dinner in Honor of Dr. Rosencrantz.—Friends and associates of Dr. Esther Rosencrantz, associate professor of medicine, University of California Medical School, San Francisco, gave a dinner at the Palace Hotel, San Francisco, July 9, to mark her retirement from the university, where she had been a member of the staff since 1913. Dr. Rosencrantz was also lecturer in medical history and bibliography in the medical school. A collector of the works of Sir William Osler, whose pupil she was at Johns Hopkins University School of Medicine, Baltimore, Dr. Rosencrantz was presented at the dinner with six rare Osler items. She has given her entire collection to the medical school.

DISTRICT OF COLUMBIA

Dr. Nichols Receives Certificate of Award.—The annual certificate of award for meritorious service to the Medical Society of the District of Columbia was recently presented to Dr. John Benjamin Nichols, who for more than forty years has rendered noteworthy service to the society. In 1912 he served as president.

FLORIDA

Personal.—Dr. Turner E. Cato has been appointed director of the Dade County Health Unit, Miami, following the recent resignation of Dr. Thomas H. D. Griffitts. Dr. Frank L. Quillman is in charge of the venereal disease division and Dr. Maryland E. B. Byrne is director of maternal and child health of the division.——Dr. Harrison A. Walker, Miami Beach, was recently named regional medical officer for the Office of Civilian Defense, Fourth Civilian Defense Region, Atlanta, Ga., succeeding Dr. Burt A. Dyar.

MASSACHUSETTS

Harvard Again Offers Course in Legal Medicine.—A seminar in legal medicine will be held in Harvard Medical School, Boston, October 4-9. Designed for medical examiners and coroners' physicians, it will be open to any other suitable graduate of an approved medical school. The course will consist of necropsy demonstrations, technic and interpretation of laboratory tests, study of the day by day cases of a medical examiner, round table conferences and the many subjects now included in the field of legal medicine. The enrolment has been limited to fifteen and the fee is $25. Applications should be made on or before October 1 to Harvard Medical School, Courses for Graduates, 25 Shattuck Street, Boston. The Massachusetts Medico-Legal Society in conjunction with the department of legal medicine of Harvard Medical School will hold an all day conference at the Mallory Institute of Pathology, Boston City Hospital, October 6. The conference will be open to any registered physician, lawyer, police official, criminal investigator, senior medical student or other person whose duties are associated with medicolegal topics. It will include lectures, demonstrations and informal discussions concerning many subjects in legal medicine, particularly stressing results of some more recent methods. No limit has been made for the number of conference attendants, there is no fee, and advance application is not essential, although it would be helpful. Address Dr. William H. Watters, Department of Legal Medicine, Harvard Medical School.

MICHIGAN

Honorarium for the Biddle Orator.—A physician who wishes to remain anonymous has set up an honorarium in the Michigan State Medical Society to be awarded each year to the person who delivers the annual Biddle Oration. Dr. Edward A. Schumann, Philadelphia, the 1943 lecturer, will deliver the oration at the annual session of the state medical society in September.

Dr. Ralph Smith Joins Louisiana Faculty.—Dr. Ralph G. Smith, associate professor of pharmacy, University of Michigan Medical School, Ann Arbor, has been appointed professor of pharmacology and head of the department at Tulane University of Louisiana School of Medicine, New Orleans. He succeeds Dr. Erwin Nelson, who recently resigned to become research director of the Burroughs Wellcome & Company (United States) experimental research laboratories at Tuckahoe, N. Y. (THE JOURNAL, July 31, p. 958). Dr. Smith graduated at the University of Toronto Faculty of Medicine in 1925.

Rejectees Examined for Tuberculosis.—Physicians qualified to interpret chest x-ray films have been named in each of fourteen districts into which the state has been divided to study chest films of rejected candidates of the armed services. The bureau of tuberculosis control of the state health department is furnished reports of local examining boards and supervises follow-up activities which secure treatment for rejectees when its need is indicated. A release from the state department of health indicates that occasionally these further studies result in reexamination and induction of men previously rejected. More often, it was stated, selectees who are turned down for induction by medical examining boards because chest films show evidence of tuberculosis are brought to the attention of health officers in their home districts, who arrange for treatment.

MINNESOTA

Kenny Institute Established.—The mayor of Minneapolis, Marvin L. Kline, announced to the press on August 5 that the Elizabeth Kenny Institute, Inc., had been created with a board of directors of ten members. The institute has been operating in Minneapolis with the assistance of the city board of public welfare. The institute is housed in a building once known as the Lymanhurst Health Center and more recently as the Public Health Center (THE JOURNAL, Dec. 5, 1942, p. 1148).

Annual Medical Meetings.—The annual meeting of the Northern Minnesota Medical Association will be held at St. Mary's Hospital in Duluth, August 28. Among the speakers will be Drs. John S. Lundy, Rochester, on "Modifications in Methods of Intravenous Anesthesia"; Walter E. Hatch, Duluth, "Status of Retrograde and Intravenous Pyelography"; Alfred W. Adson, Rochester, "Current Economic Problems," and Lieut. Col. Robert B. Radl, M. R. C., St. Paul, "Medical Problems of Selective Service and the Army." At the annual session of the Southern Minnesota Medical Association in the Austin Central High School, Austin, August 23, the speakers will include Drs. Karl H. Pfuetze, Cannon Falls, on "Intrapleural Pneumolysis"; Dewey E. Morehead, Owatonna, "Dührssen's Incisions," and Nelson W. Barker, Rochester, "Use of Anticoagulant Drugs, Heparin and Dicumarol, in Medicine and Surgery." There will also be a round table discussion on weakness.

NEW YORK

Orchestra Founded by Physician.—For thirty-nine years members of an orchestra started by Dr. Leonard G. Stanley, Albany, have been meeting every Thursday night, except during June, July and August. The orchestra has never given a public performance. At one time the orchestra included, with Dr. Stanley, three physicians, one of whom was the late Dr. Howard E. Lomax of the Albany Medical College. Dr. John H. Gutmann, Albany, retired because of ill health. Dr. Stanley, who is 73 years of age, is the conductor of the group.

Hospital News.—Construction started, June 15, on a new $40,000 addition to the Margaretville Hospital, Margaretville. The addition will increase the bed capacity from twelve to twenty-five single rooms and will also include two 6 bed wards, two new nurseries, a new operating room suite and a new delivery suite as well as a modernized laboratory and diagnostic facilities. The addition will bring to the top bed capacity to 62 beds in case of emergency with a normal quota of 37. Funds for the new addition are being raised through popular subscription and it is expected that the construction will be completed about December 1. Dr. Gilbert M. Palen has been appointed chief of the medical and surgical staffs and Dr. Gilbert J. Palen superintendent.——The Sister Elizabeth Memorial, first maternity hospital in Bay Ridge, was dedicated on July 11; the hospital is a division of the Norwegian Lutheran Deaconesses' Home and Hospital, Brooklyn, and was named in honor of the first head deaconess of the hospital, the late Sister Elizabeth. It has 40 beds and eight nurseries and was equipped at a cost of about $110,000.

New York City

Nutrition Center Opened.—A food and nutrition center, to be the headquarters of the New York City Food and Nutrition Program, was formally opened on July 28 at 45 Lafayette Street, Manhattan. The center primarily will be an information bureau where persons may receive free nutrition advice keyed to the latest wartime market conditions. It will also serve as a center where the contributions of the participating agencies can be made available to the public. Dr. Ernest L. Stebbins, city health commissioner, presided at the opening and speakers included Mayor Fiorello H. LaGuardia and Grace MacLeod, Ph.D., professor of nutrition at Teachers College.

Grant to Aid Neuropsychiatric Rejectees.—The State Charities Aid Association has received a grant of $19,000 from the Commonwealth Fund to enable its city mental hygiene commission to prepare a plan for aiding men rejected or discharged by the armed forces because of neuropsychiatric conditions. The money became available on July 1. In a statement to the press, as reported in the New York *Times*, July 10, Homer Folks, secretary of the State Charities Aid Association, suggested that the problem of providing psychiatric and other needed help for rejected and discharged men was of too great magnitude for any voluntary organization or organizations to solve. At the same time the State Charities Aid Association "might perform a very useful service in defining much more clearly the extent and character of the need of these two groups of men, determining what sorts of help are needed, how such help could be provided by some public authority, and what the cost would be."

NORTH CAROLINA

Special Society Election.—Dr. Romulus L. Carlton, Winston-Salem, was elected president of the North Carolina Tuberculosis Association at its meeting in Raleigh recently. According to the state medical journal, other officers include Dr. David T. Smith, Durham, vice president; Dr. Joseph J. Combs, Raleigh, treasurer; Mrs. Marie B. Noell, Raleigh, secretary, and Frank W. Webster, Raleigh, executive secretary.

Personal.—Sterling Brackett, Ph.D., assistant professor of public health in the School of Public Health of the University of North Carolina, Chapel Hill, has been appointed malariologist in the Stamford Research Laboratories of the American Cyanamid Company, Stamford, Conn.——Dr. Charles W. Banner, Greensboro, was honored recently when a large portrait of him was presented to the L. Richardson Memorial Hospital, Greensboro. Dr. Banner is chairman of the board of trustees of the hospital.

OHIO

Opposition to Medical Program for Families of Service Men.—At a meeting, July 11, the council of the Ohio State Medical Association adopted a statement of policy, recommending methods of assisting needy wives and infants of enlisted men in the armed forces to obtain financial assistance for medical and nursing services and hospitalization, if the need for such financial assistance arises, and opposing a plan proposed by the U. S. Children's Bureau for the establishment of a federally financed and supervised medical program in Ohio. Before the use of public funds or the maintenance of a government controlled medical program to furnish this type of service is made necessary, the association recommends cooperation with the army emergency relief and similar agencies in other services which already have funds available for immediate need. In offering its recommendations the Ohio State Medical Association urges its members to see "that all persons regardless of financial status shall be provided with an opportunity to utilize the advantages of modern scientific medicine" at this time.

PENNSYLVANIA

Protest Appointment of Layman in Health Job.—Physicians have been protesting to their local societies against the appointment by Governor Martin of Carl C. Tinstman, Forty Fort, as deputy secretary of health. The Dauphin County and Perry County medical societies have adopted resolutions protesting to the state medical society the selection of a layman for this position, which has been filled by a "medical man since the creation of the state health department in 1905."

Philadelphia

Osler Medal Goes to Pennsylvania Student.—The American Association of the History of Medicine has awarded the William Osler Medal to Dr. George E. Murphy, Kansas City, Kan., 1943 graduate of the University of Pennsylvania School of Medicine, in recognition of his essay "The Evolution of Our Knowledge of Rheumatic Fever." The essay is to be published in the *Bulletin of the History of Medicine*. The Osler Medal was established in 1941 to be awarded for the best student essay submitted to the association (THE JOURNAL, Oct. 25, 1941, p. 1482).

Dean Sturmer Retires.—Julius W. Sturmer, Phar.D., has retired as dean at the Philadelphia College of Pharmacy and Science after serving in this capacity since 1916. After Dr. Sturmer graduated at Purdue in 1891 he served for a number of years as a member of the faculty. In 1912 he became professor of pharmacy and dean of pharmacy at the Medico-Chirurgical College of Philadelphia. In 1916, after the merger of this college with the University of Pennsylvania and following an agreement with the Philadelphia College of Pharmacy involving the transfer of pharmacy students of the Medico-Chirurgical College to the Philadelphia College of Pharmacy, Dr. Sturmer became professor of pharmaceutical chemistry and a dean in the latter institution. With the establishment of the curriculum in chemistry, bacteriology and biology in 1921 the college changed its title to the Philadelphia College of Pharmacy and Science and Dr. Sturmer became its dean of science.

RHODE ISLAND

Medical News to Merge with State Journal.—The *Providence Medical News* suspended publication with its July issue to merge with the *Rhode Island Medical Journal*. The Providence Medical Association published its first journal in January 1900 as a quarterly, relinquishing its ownership in 1917 in order that the journal might become a monthly publication under the auspices of the state medical society. In May 1939 the association created the *Providence Medical News*, and it is this publication that is now being combined with the state medical journal.

No Award of Fiske Fund.—The *Rhode Island Medical Journal* has announced that the income of the funds making up the Fiske Award is not enough to offer any premium this year or to carry on any of the former activities of the fund. The money was left by Dr. Caleb Fiske to encourage original work on the part of the members of the society. Amounting to $12,000, these funds are invested by court order in such a way that the income, under present conditions, is almost negligible. The trustees are attempting to have the investments changed to bring about a reasonable return, assuring the continuance of the fund's work next year.

State Medical Election—Dr. Elihu S. Wing, Providence, is the president-elect of the Rhode Island Medical Society and Dr. Michael H. Sullivan, Newport, chosen vice president, was elevated to the presidency, filling the vacancy that occurred with the death of Dr. Murray S. Danforth, Providence, three days after his installation as president of the society. Dr. James L. Wheaton, Pawtucket, was named vice president. Dr. William P. Buffum, Providence, is the secretary, Dr. Albert L. Potter, Providence, assistant secretary and Dr. Jesse E. Mowry, Providence, treasurer. Mr. James E. Farrell is the new executive secretary. Dr. Edwin H. Place, professor of clinical pediatrics, Tufts College Medical School, Boston, delivered the annual Charles V. Chapin Oration during the meeting on "Changing Views of the Contagious Diseases." Other speakers on the program included:

Dr. Anthony V. Migliaccio, Providence, Report of Six Cases of Meckel's Diverticulum.
Lieut. Col. Marshall N. Fulton, M. C., A. U. S., The Problems of an Army General Hospital.
Major Clarance E. Bird, M. C., A. U. S., The McBurney Incision.
Dr. Alexander T. Martin, New York, Rheumatic Fever in Children, Its Recognition and Management.

TENNESSEE

Dr. Christie Succeeds Dr. Casparis.—Dr. Amos Christie, assistant medical director of the American Red Cross, Washington, D. C., has been appointed professor of pediatrics at Vanderbilt University School of Medicine, Nashville, succeeding the late Dr. Horton R. Casparis. Newspapers report that Dr. Christie will begin his new work on October 1. Prior to his appointment with the Red Cross, Dr. Christie had been connected with the University of California Medical School, San Francisco, since Sept. 1, 1930 and most recently as associate professor of pediatrics. He had also been a member of the California State Board of Health and once served as specialist in pediatrics with the U. S. Children's Bureau.

TEXAS

Dr. Thompson Made Member Emeritus.—At the recent annual meeting of the State Medical Association of Texas, Dr. William R. Thompson, Fort Worth, was elected a member emeritus of the association. Dr. Thompson is the only living member of the original board of trustees of the association, having been a member since 1904. He had been secretary of the board of the association from 1905 to 1942.

Memorial Library Funds.—Dr. Judson L. Taylor, Houston, immediate past president of the State Medical Association of Texas, jointly with Mrs. Taylor has set up two memorial funds for the support of the Texas Memorial Medical Library Association. One fund commemorates the medical service of Dr. Taylor's brother, Dr. Martin Junius Taylor, now living in Houston, and the other is in memory of Mr. and Mrs. William Thomas Carter, the parents of Mrs. Taylor.

Construction on Cancer Project.—The clinic buildings for the M. D. Anderson Cancer Research Hospital are being erected at 2310 Baldwin Avenue, Houston, where the old Baker Home has been in use for quarters of experimentation for the last three months, the *Texas State Journal of Medicine* reported in July. There will be three buildings, a reception center, an animal house and a biochemistry building, all of which are expected to be available within the next three months.

Lectureship in Ophthalmology to Honor Dr. McReynolds.—Mrs. F. W. Wozencraft, Washington, D. C., has presented a fund to establish a lectureship in ophthalmology at the University of Texas Medical Branch, Galveston, in honor of her father, Dr. John O. McReynolds, who died on July 7, 1942. Dr. McReynolds, who entered private practice in Dallas in 1892, was Vice President of the American Medical Association in 1926-1927 and chairman of the Section on Ophthalmology, 1922-1923.

Storm Forces Cancellation of Graduation Exercises.—The fifty-third graduation exercises of the University of Texas Medical Branch, Galveston, scheduled for Saturday, July 31, were canceled because of the damage caused by a tropical storm, according to an announcement from Chauncey D. Leake, Ph.D., dean. Degrees were conferred on August 2 just prior to the beginning of the state board examinations and diplomas were presented August 4 at an informal meeting at which Dr. Witten B. Russ, San Antonio, spoke on "The Doctor and the Postwar World."

UTAH

State Medical Meeting.—At the annual session of the Utah State Medical Association at the University of Utah, Salt Lake City, August 27-28, speakers will include:

Dr. Emil G. Holmstrom, Salt Lake City, Treatment of Carcinoma of the Cervix Uteri.
Dr. Adelbert Louis Dippel, Minneapolis, Some Aspects of a Statewide Maternal Mortality Study.
Lieut. Col. James S. Sweeney, Paris, Texas, M. C., A. U. S., The Peptic Ulcer Syndrome in Patients Without Radiographic Evidence of Ulcer.
Major Rudolph A. Kocher, Carmel, Calif., M. C., A. U. S., Malaria in Soldiers Returned from the Southwest Pacific.
Lieut. Col. Henry G. Hollenberg, Little Rock, M. C., A. U. S., Treatment of Wounds: Consideration of General Nutritional Disturbances and New Therapeutic Agents Such as Penicillin.
Dr. John Z. Brown, Salt Lake City, Report of Delegate to the American Medical Association.
Dr. Lynne A. Fullerton, Denver, Senior Surgeon, U. S. P. H. S., Some Public Health Problems in Utah.
Lieut. Col. Harold R. Hennessy, Salt Lake City, M. R. C., U. S. Army, The Industrial Medical Program of the United States Army.
Dr. Philip B. Price, Baltimore, Hand Disinfection.
Lieut. Col. John B. Flick, Bryn Mawr, Pa., M. C., A. U. S., Treatment of Burns.
Lieut. Col. Verne R. Mason, Los Angeles, M. C., A. U. S., and Major William J. Mitchell, Los Angeles, M. R. C., U. S. Army, Therapeutics in Army Hospitals.
Lieut. Woodrow W. Schier, Manhasset, N. Y., M. C., A. U. S., Aviation Medicine—Problems of High Altitude Flying.
Dr. Fuller B. Bailey, Salt Lake City, Diarrhea.
Lieut. Col. Olin B. Chamberlain, Charleston, S. C., M. C., A. U. S., The Concept of Psychosomatic Medicine.

WISCONSIN

State Medical Meeting.—The one hundred and second annual meeting of the State Medical Society of Wisconsin will be held in Milwaukee, September 13-15, under the presidency of Dr. Russell M. Kurten, Racine, with sessions in the Milwaukee Auditorium and Hotel Schroeder. The program will include the following out of state speakers:

Dr. Frank C. Mann, Rochester, Minn., Physiology of the Liver.
Dr. Cecil J. Watson, Minneapolis, Studies of Liver Disease with Correlation of Clinical Features and Liver Function Tests.
Dr. Marion A. Blankenhorn, Cincinnati, Differential Diagnosis of Jaundice.
Dr. Warren H. Cole, Chicago, Surgical Advances from the War.
Rear Admiral Ross T. McIntire, surgeon general of the U. S. Navy, The Navy's Demand on the Scientific Training of the Medical Officer.
Dr. George B. Eusterman, Rochester, The Relation of Peptic Ulcer to Cancer of the Stomach.
Dr. Donald C. Balfour, Rochester, When Is Peptic Ulcer a Medical and When Is It a Surgical Problem?
Dr. Frederick A. Coller, Ann Arbor, Mich., Transfusions and Fluid Balance.
Dr. John Romano, Cincinnati, Psychiatric Problems Arising from Military Service.
Dr. Claude F. Dixon, Rochester, Diagnosis and Treatment of Cancer of the Bowel.
Dr. John S. Coulter, Chicago, Medical Aspects of Chemical Warfare.
Dr. William A. O'Brien, Minneapolis, Problems Concerning Graduate Education and Employment of Nurses, Interns and Residents.
Mr. J. W. Holloway Jr., director, Bureau of Legal Medicine and Legislation, American Medical Association, Chicago, Hospitals in the Selection of Medical Staffs.
Father Alphonse M. Schwitalla, S.J., Ph.D., St. Louis, Future Joint Problems of Medicine and the Hospitals.
Dr. Chauncey C. Maher, Chicago, Recognition of Early Myocardial Failure.
Dr. Paul S. Rhoads, Evanston, Ill., Rheumatic Fever: Diagnosis and Treatment.
Dr. Ralph A. Reis, Chicago, Sterility.
Dr. Sanford R. Gifford, Chicago, The Eye in General Diagnosis.
Dr. Hart E. Van Riper, Washington, D. C., Better Health for Children: Physicians and the Social Security Program.
Dr. Paul H. Holinger, Chicago, The Infant Larynx.
Dr. Edgar J. Huenekens, Minneapolis, Immunization in Pediatrics Practice.
Dr. Leo M. Zimmerman, Chicago, Improved Surgical Treatment of Hernias.
Dr. James B. Brown, St. Louis, Plastic Surgery.
Dr. Dean M. Lierle, Iowa City, Iowa, Acute Upper Respiratory Infections and Their Control.
Dr. John L. Emmett, Rochester, Treatment of Urinary Stones.
Dr. Charles D. Creevy, Minneapolis, Urinary Diagnosis.
Capt. William E. Eaton (MC), U. S. Navy, Ulcer Problem in the Armed Forces.

GENERAL

Infantile Paralysis Fund Collections.—A total of $5,527,590.99 was collected in the annual appeal for infantile paralysis funds, exceeding by more than 30 per cent all previous collections. The total was $1,500,000 higher than any previous year. Expenses were $147,871.41, or only 2.6 per cent of the collections, less than half the cost in any other year in the decade that President Roosevelt's birthday has been dedicated to the fight against poliomyelitis, according to the National Foundation for Infantile Paralysis.

Fourth of July Deaths Reduced.—Reports assembled by the Associated Press indicated that the traffic deaths throughout the nation over the Fourth of July weekend dropped by more than half as compared to last year while railroad travel reached record proportions, according to the New York *Times*. The tally of highway fatalities was 131 as against 320 last year and 500 in 1941, which was before the institution of gasoline rationing. Deaths due to fireworks were reduced to zero. The total of deaths from all causes was listed as 307, 89 of the remainder being drownings and the rest miscellaneous.

Prize for Paper on Glaucoma.—The National Society for the Prevention of Blindness announces that a prize of $250 will be awarded for the most original paper adding to the present knowledge about medical treatment of noncongestive glaucoma. This prize is being offered in addition to one that was previously announced for the most valuable original paper concerning the early diagnosis (THE JOURNAL, Dec. 12, 1942, p. 1238). Papers may be presented by any practicing ophthalmologist in the Western Hemisphere and may be written in English, French, German, Italian, Spanish and Portuguese, but any of those written in the last four languages should be accompanied by an English translation. The award will be made by the society with the guidance of an ophthalmologic committee. Papers should be in the office of the society, 1790 Broadway, New York, by September 1944.

National Research Council Fellowships.—Recent fellowships announced by the medical fellowship board of the National Research Council, Washington, D. C., include the Welch fellowships in internal medicine to Dr. Sinclair Howard Armstrong Jr., Harvard Medical School, Boston, and Dr. Joseph F. Ross, Robert Dawson Evans Memorial Hospital, Boston. A fellowship in the medical sciences was renewed for Dr. Lester

J. Talbot at the New York University College of Medicine, and one for orthopedic surgery for Dr. Maxwell F. Kepl at Tulane University of Louisiana, New Orleans. Fellowships in filtrable viruses were awarded to Edward H. Anderson, Ph.D., Vanderbilt University; H. Chandler Elliott, Ph.D. (renewal), University of Toronto; Dr. I. William McLean Jr., Duke University School of Medicine; Dr. Alison H. Price, University of Michigan (declined appointment); Dr. Hugh Tatlock, Yale University School of Medicine, New Haven, Conn., and the Acute Respiratory Diseases Commission Laboratory, Fort Bragg, N. C., and Dr. Herbert A. Wenner, Yale University School of Medicine and Johns Hopkins University.

Distribution of Excessive Poliomyelitis.—The following tabulation presents the available figures for areas in which poliomyelitis is known to have reached excessive proportions:

	Cases Reported 1943 up to Aug. 7	Cases Reported Week Ended Aug. 7
1. Alabama	46	6 (July 31)
2. California	952	111
Kern County (week ended July 31)	108	46
Los Angeles County (week ended July 31)	231	28
3. Connecticut	41	24
New Haven County	34	20
4. Kentucky	51	8
5. Oklahoma	292	52
6. Texas	757	62
Dallas County (week ended July 31)	60	10
Harris County (week ended July 31)	81	10
Tarrant County (week ended July 31)	80	12

There is reason to believe that the incidence of poliomyelitis may be considerably above normal in some other areas, notably Kansas, but figures for Kansas were not available.

Other areas under suspicion are:

	1943 to July 24	Week Ended July 24
Washington	22	2
	1943 to Aug. 16	Aug. 1 to Aug. 17
Illinois	134	124
Cook County	...	113

Congress of Physical Therapy.—The American Congress of Physical Therapy will hold its twenty-second annual session at the Palmer House, Chicago, September 8-11. At the formal opening the speakers will include Drs. Kristian G. Hansson, New York, on "Physical Therapy in Wartimes" and Eben J. Carey, Milwaukee, "Physical Therapy in Medical Education." Among the other speakers on the program will be:

Capt. Sidney H. Licht and Capt. Vernon S. Dick, M. C., A. U. S., Sulfadiazine and Fever Therapy in Resistant Gonorrhea.
Lieut. Comdr. Kenneth Phillips (MC), U. S. Naval Reserve, and Ensign Alice B. Mundorff (NC), U. S. Naval Reserve, The Reduction of Man Power Loss from Gonorrheal Urethritis by the Early Application of Chemo-Fever Therapy.
Lieut. Arthur Price, M. C., A. U. S., Renal Complications in Combined Sulfathiazole-Fever Therapy.
William Firth Wells, B.Sc., Philadelphia, Radiant Disinfection.
Drs. George P. Miley, Jens Allen Christensen and Raymond Edwin Seidel, Philadelphia, A Preliminary Report of Results Observed in Eighty Cases of Intractable Bronchial Asthma.
Dr. Robert Talbot McElvenny, Chicago, Refrigeration.
Dr. Bayard T. Horton, Rochester, Minn., Peripheral Vascular Disease.
Dr. Hans J. A. Behrend, New York, Modern Hydrotherapy: II. A Review of Recent Developments.
Dr. Carl E. Badgley, Ann Arbor, Mich., Rehabilitation of Arthrogryposis Multiplexa Congenita.
Dr. Edward L. Compere, Chicago, Management and Care of Infantile Paralysis Patients.
Dr. Madge C. L. McGuinness, New York, Rehabilitation, Prehabilitation and Placing the Recovered Workman.
Dr. Alfred P. Solomon, Chicago, Psychiatric Orders for Rehabilitation Physical Therapists.
Dr. Edward C. Holmblad, Chicago, Rehabilitation of Injured Workers in Small Plants.
Dr. Geza de Takats, Chicago, Sudeck's Atrophy—A Chronic Vasodilator Mechanism.
Dr. Jessie Wright, Pittsburgh, Mechanics in Relation to Derangement of the Facet Joints in the Spine.
Dr. Clarence A. Neymann, Chicago, Some Thoughts About Shock Therapy.
Dr. John A. Aita, Rochester, Electric Shock Therapy, Its Indications and Use.
Dr. Edgar V. Allen, Charles Sheard, Ph.D., and Grace M. Roth, Ph.D., Rochester, The Interpretation and Clinical Significance of Calorimetric and Skin Temperature Measurements of the Extremities.
Brig. Gen. Frank T. Hines, Washington, D. C., Rehabilitation in the Veterans Administration.
Major Ora L. Huddleston, M. C., A. U. S., Use of the Convalescent Ward in the Rehabilitation and Disposition of Disabled Soldiers.
Lieut. Comdr. Jacob L. Rudd (MC), U. S. Naval Reserve, Rehabilitation of War Wounded in a Physical Therapy Department of a Navy Hospital.
Dr. Frank H. Krusen, Rochester, Physical Rehabilitation and the War.
Lieut. Comdr. Louis B. Newman (MC), U. S. Naval Reserve, Organization and Management of a Navy Physical Therapy Department.
Dr. Warren H. Cole, Chicago, The Treatment of Shock, With Special Reference to Heat and Cold.
Dr. Harry E. Mock, Chicago, Rehabilitation in Head and Back Injuries.

There will also be a symposium on "Rehabilitation of the Child," an instruction seminar, and demonstration. Additional information may be obtained from the executive director, American Congress of Physical Therapy, 30 North Michigan, Chicago.

LATIN AMERICA

The Brazilian Book of Honor.—The name of Dr. Vital Brasil, at one time inspector of public health in São Paulo and founder of the Vital Brasil Institute of Niteroi, Rio de Janeiro, for the preparation of serum and vaccines and for research work, has been added to the Brazilian "Book of Honor," established recently by Dr. Getulio Vargas, president of Brazil, to preserve the names of great Brazilians for posterity.

Latin American Congresses.—The seventh Argentine Congress of Medicine will meet in La Plata City, November 14-21. The headquarters of the congress are Calle 50 número 374 La Plata, Argentina, S. A.——The first Inter-American Congress of Radiology will meet in Buenos Aires during the last two weeks of October. Dr. José F. Merlo Gómez, the president of the Sociedad Argentina de Radiología, and Dr. Oscar F. Noguera will be the president and general secretary, respectively. Drs. Sabina di Rienzo of Cordoba, Luis Opazo and Leonardo Guzman C. of Chile, Nelson de Carvalho of Brazil, Pedro A. Maissa of Buenos Aires, Gonzalo Esguerra Gómez of Bogotá and Oscar Soto of Lima will be official speakers. The headquarters of the congress are as follows: Secretaría General del Primer Congreso Inter-americano de Radiología, calle Alsina, 3317, Buenos Aires, Argentina, South America.

Establish Laboratory in Dominican Republic.—Dr. Enrique W. Lithgow, who has for two years been associated with the pathology department of Mount Sinai Hospital, left New York on August 2 to establish a pathologic laboratory and postgraduate educational program in pathology in the Dominican Republic. Dr. Lithgow's study at Mount Sinai has been financed by the Dazian Foundation. Recently Dr. Fernando A. Batlle, director of the Padre Billini hospital and president of the Cancer Institute in Trujillo City, invited Dr. Lithgow to return to his native land to make available there the benefits of current advances in pathology. This invitation was supported by the Dominican government. He will take up research and educational activities at the Padre Billini Hospital and later at the Cancer Institute, which is to open in the near future. The fellowship under which Dr. Lithgow was working is one of several granted annually by the Dazian Foundation under the presidency of Dr. Emanuel Libman, consulting physician to the hospital, which are awarded to selected younger physicians of Central and South American countries for postgraduate study and research in the United States.

FOREIGN

Distribution of Medical Journals to Chinese Institutions.—A case containing six sets of medical journals sent by the American Bureau for Medical Aid to China, recently received in Chungking, was distributed by Surgeon General Loo Chi-teh so that it will serve about eighteen separate institutions. One set went to the Emergency Medical Service Training Schools. Another was sent to Koloshan, where it will be available to the Shanghai Medical School, the National Institute of Health, the Central Hospital and the Nursing School. The set at Kweiyang will serve Hsiang Ya and Kweiyang Medical Schools, the Provincial Health Department and the Training Institute. To Chengtu went one set for the use of National Central Medical School, West China University, the Branch Training School, Provincial Health Department and the editors of the *China Medical Journal*. The Army Medical College at Anshun received a set, while the remaining one went to the northwest for the training schools, Epidemic Prevention Bureau, Northwest Hospital and Kanus National Medical College. In this way the medical literature sent by the American Bureau for Medical Aid to China benefits the greatest possible number of people, according to an announcement.

Deaths in Other Countries

Sir Harold Beckwith Whitehouse, president of the British Medical Association, professor of midwifery and diseases of women, University of Birmingham, died in London on July 28, aged 60. According to the New York *Times*, Sir Harold collapsed on the street just after leaving the British Medical Association meeting, at which he had been nominated for the presidency for the second successive year. He died one hour later. In 1933 he was a visitor to the United States as the guest of the American College of Surgeons.

Foreign Letters

LONDON

(From Our Regular Correspondent)

June 15 (delayed).

The Army Blood Transfusion Service

The British army has a highly developed blood transfusion service. Its headquarters were established in England six months before the war and its plasma drying plant was erected in 1941. In England the service operates in 850 centers with a staff of 350, of whom more than three fourths are women. The original technical staff was drawn largely from the technical staffs of the Royal College of Surgeons and the Middlesex Hospital. The Army Blood Supply Depot has a panel of over 200,000 donors and collects 3,000 pints of blood a week. The blood is issued to all theaters of war either as stabilized fluid plasma or as the dried product, which keeps indefinitely. Whole blood of group O is supplied only to units which have a refrigerator. Before issue it is tested to make sure of the grouping and also to exclude syphilis. Blood banks, consisting of blood dispatched from the central depot to a peripheral point, need close attention to avoid undesirable reactions. Bank blood must never be allowed to warm until just before administration, for a high proportion has been found to contain a few nonpathogenic organisms. Though insignificant as long as the blood is kept cool, they multiply rapidly on warming. The ideal temperature for the refrigerator is 4 to 6 C. Too low temperatures tend to cause rapid hemolysis.

The arrangements in the field are described in the Army Medical Department Bulletin. Where lines of communication exist, field transfusion units are supplied from the base. In addition all medical units carry a "field medical box" containing transfusion fluids ready for immediate use. When lines of communication are interrupted, units which have exhausted their stocks of transfusion fluids and cannot get fresh supplies must collect blood from volunteers. The "field transfusion box" contains equipment for bleeding donors and for ascertaining their blood groups; but when it is anticipated that medical units will be working in isolation the whole personnel may be grouped in advance, so that any one can serve as a donor without further test. Similarly, certain combatant formations, such as commando and air borne troops, are grouped so as to minimize delay in finding donors suitable to each patient. When temporary isolation is expected, medical units can carry specially prepared large stocks of prepared fluids, and further supplies may be dropped by parachute.

The European Association of Clinical Pathologists

One result of the war is much increased personal contact of our physicians with those of the allied countries who are refugees here. This has resulted in the formation of a new body, the European Association of Clinical Pathologists, which is to function permanently after the war. At a meeting held in London the following officers were elected: president, Dr. S. C. Dyke, England; vice president, Prof. E. J. Bigwood, Belgium; secretary, Dr. F. Pick, Czechoslovakia; treasurer, Dr. B. L. Della Vida, Italy; council, Dr. A. Benau, Yugoslavia; Dr. D. C. Canne, Netherlands; Dr. F. Duran-Jorda, Spain; Prof. F. Silberstein, Austria; Dr. G. Ungar, France, and Dr. J. Ungar, Czechoslovakia. The annual subscription, including the entrance fee, is $2. Rules were adopted for the association while its members are mainly in this country, and the council was instructed to consider the procedure to be adopted after the liberation of Europe. A resolution was passed to the effect that free interchange of workers in clinical pathology between the nations of Europe would be an important factor both in the advancement of scientific medicine and in the development of a common European mentality, these being the main objects of the association. An invitation was received from the British Association of Clinical Pathologists inviting members of the European association to participate in its meetings. Membership is open to physicians of all European nationalities engaged in any form of medical laboratory work. Those interested are invited to communicate with the secretary, Dr. Pick, Department of Clinical Pathology, General Hospital, Walsall, Staffs, England.

A British Hospital for Stalingrad

The archbishop of Canterbury, Lord Horder, Sir Gowland Hopkins and other well known persons have published an appeal for funds to build a new hospital at Stalingrad as "a permanent expression of the British people's gratitude to the defenders of Stalingrad, who have made such a great contribution to the final victory of the united nations." The Joint Committee for Soviet Aid is appealing for $375,000 by June 22. The *British Medical Journal* suggests that if every one on the Medical Register should contribute $4, this aim would be achieved without further contributions. But much more than the sum mentioned will be required to complete a hospital which will be a fitting memorial to the defenders of Stalingrad and at the same time play a large part in supplying the needs of that historic city.

Constantine Lambrinudi: A Great Orthopedic Surgeon

The death at the age of 53 of Constantine Lambrinudi has cut short the career of a leader in orthopedics much esteemed for his personal qualities. The son of a Greek stockbroker settled in London, he was educated at Cambridge and Guy's Hospital. His studies were interrupted by service in a Red Cross unit in the Greco-Bulgar campaign and then as an unqualified doctor in the Greek army. After qualifying in 1914 he joined the army of Venizelos. Toward the end of the first great war he became a medical officer in the British air force. In 1928 he was appointed assistant orthopedic surgeon to Guy's Hospital and in 1934, on the death of Mr. Trethowan, orthopedic surgeon in charge of the department. An original thinker on the lines of function, he worked out the cause and correction of deformities. Present day views on the mechanism of the foot are due to his teaching. He is remembered for his operation for drop foot, his treatment of claw toes by arthrodesis, his operation for elevated first metatarsal with hallux rigidus and the use of Kirschner wires for fixing certain fractures. A keen advocate of correct posture, he was the first to show the connection between short hamstrings and adolescent kyphosis. As a teacher of orthopedics he was supreme. His originality and quick insight impressed those who had the good fortune to be his pupils. In a tribute published in the *Guy's Hospital Gazette* he is described as possessed of the power to see things anew with a vision entirely unprejudiced by established beliefs. He always laid stress on function and therefore instituted the employment of a visiting masseuse in hospital practice.

Faculty of Medicine of the University of Poland Within Edinburgh University

The Faculty of Medicine of the University of Poland was established within the University of Edinburgh for the exiled Poles so as to keep together professors, physicians and other medical workers, to give them an opportunity for research and teaching and generally to promote the academic spirit, so that after the war Poland would have at least one active medical school. All those in Poland were destroyed by the Germans. The project has been successful and a Polish hospital is attached to the school for clinical work. The course of study and the examinations are arranged in accordance with the

requirements of Polish law and at the same time to approximate as much as possible Edinburgh standards. A ceremony has taken place in which representatives of the University of Edinburgh and the Polish Faculty of Medicine attended. The president of the republic of Poland conferred the Order of Polonia Restituta on Sir Thomas Holland, vice chancellor and principal of the University of Edinburgh; Prof. Sidney Smith, dean of the Faculty of Medicine, and Prof. F. A. E. Crew, who holds the chair of genetics. This was done in recognition of the great service rendered to Poland by the university in giving an invitation to found a technical school within its walls.

AUSTRALIA

(From Our Regular Correspondent)

June 30, 1943.

Social Trends in Australian Medical Practice

THE NEW ZEALAND SCHEME

Medical benefits as incorporated in the National Health and Pensions Act of 1938 and the report of the Federal Council of the British Medical Association in Australia have been discussed in previous letters. The third scheme for an Australian Medical Service under consideration is that now operating in New Zealand. The New Zealand Social Security Bill was passed in 1938. It was intended to provide a system of monetary and of medical, hospital and related benefits on a contributory basis. The scheme was financed by a new social security tax, which has been in operation since April 1939. Maternity, hospital, pharmaceutic, radiologic and medical benefits were instituted in this order during the period dated from April 1939 to December 1941. The general practitioner service originally promulgated in March 1941 was based on a capitation system. The medical profession refused to cooperate, and in December 1941 the government was forced to introduce an alternative "fee for service" scheme.

The benefits now in operation include the following:

(*a*) Maternity Benefits: Doctors receive £5-5-0 from a social security fund for each confinement with extra for anesthetics. Recognized specialists are allowed to charge their usual fee and collect the difference from the patient. All practitioners except those who do not ordinarily practice midwifery are considered to be working under the scheme. The maternity hospitals normally receive £11 11s. for each confinement, but some hospitals, by special permission of the government, are allowed to charge more.

(*b*) Hospital Benefits: Public hospital services, including accommodation, maintenance and medical attendance, are free to all sections of the community. Public and private hospitals receive 6 shillings a day per occupied bed from the social security fund.

(*c*) Pharmaceutic and Roentgenologic Benefits: Drugs and preparations appearing in the British pharmacopeia are free. Roentogenologic services at public hospitals are free; private radiologists charge a stipulated fee, of which the government and the patient each pay half.

(*d*) General Practitioner Service: There are two schemes in operation: (1) Doctors may take at a capitation of 15 shillings a head per year up to 4,000 on a panel or (2) they may charge as much as 10/6 per service, of which 7/6 is paid from the social security fund. An extra charge is made for mileage in country districts. Only a very few medical practitioners work under the capitation system.

(*e*) Specialist Services: These are free at public hospitals; private patients may claim 7/6 out of the usual specialist fee of £1 1s.

The New Zealand scheme is a socially valuable one in that it has ensured medical attendance for every member of the community. But, by stabilizing the economic aspect of medical practice for both patient and professional, it has tended to establish medical efficiency generally at the level which existed prior to its introduction. In the latter respect the scheme is static, in that it offers no constructive policy for maintaining or improving the standard of medical practice, and retrogressive, in that it has done little to abolish preexisting evils of medical organization and administration. Under the scheme no help is given toward the cooperation of doctors in groups for mutual relief and better service. No provision is made for postgraduate training or large scale research operations and there is no comprehensive scheme for including the newer tendencies of modern preventive medicine in the general medical service. The deficiencies of the scheme are well exemplified by a consideration of hospital services. Many public hospitals, especially those in large cities, are out of date, ill equipped and not necessarily staffed by the best medical talent of the district. Owing to the shortage of hospital accommodation the provision of free hospital service is often an illusory one; patients may have to wait months before being admitted. The scheme has led to a greater use of private hospitals and nursing homes, and the position of many small inefficient hospitals has been confirmed. Private hospital fees have risen in consequence.

Up to the present the scheme has shown too many defects to be regarded as an ideal basis for a general medical practice for the community, but it is possible that in time a more progressive and constructive scheme may be evolved out of that at present in operation.

Exemption for Students

In order to ensure a steady flow of trained professional men to meet the requirements of the services and the increased demands of the postwar period, action has been taken by the manpower authorities to exempt certain classes of students from call ups for compulsory military service. The director general of manpower has announced that all full time students accepted by a university in the faculties of medicine, science (including pharmacy), engineering, dentistry, agricultural science and veterinary science are totally reserved. As far as the medical profession is concerned, it is of paramount importance that there should be sufficient numbers of trained personnel to meet the increased demands which the proposed national health services must necessarily place on the profession. There must, however, be a limitation and control of the number of admissions to the reserved faculties to guard against an unwarranted influx of students seeking to avoid military service. A workable plan must be devised for securing the best material and allocating it to the best advantage.

Marriages

THOMAS MICHAEL HUGHES, Columbus, Ohio, to Miss Dorrith Ramona Abegglen of Tekoa, Wash., in San Diego, Calif., June 15.

WILLIAM EDWARD BALDWIN JR., Dunn, N. C., to Miss Martha Virginia Dixon of Pisgah Forest, July 2.

HENRY B. DIVERTY, Woodbury, N. J., to Miss Jeanette Lee Livingston of Middletown, N. Y., July 9.

ROBERT WILSON KING to Miss Dorothy Williamson Sisk, both of Fayetteville, N. C., July 13.

THOMAS P. WARING JR., Savannah, Ga., to Dr. RUTH MOYER of Baraga, Mich., July 11.

CHARLES M. HARRIS JR. to Miss Margaret Ann Holland, both of Atlanta, Ga., July 3.

JOHN SHEDD SCHWEPPE, Lake Forest, Ill., to Miss Lydia H. Elliott of Winnetka, July 17.

IRWIN M. MARCUS to Miss Phyllis Harriet Pincus, both of Chicago, June 23.

JOHN R. U. CAMPBELL, Gilroy, Calif., to Mrs. Kay Christie recently.

Deaths

Arthur Thomas McCormack ✠ widely known as secretary of the Kentucky State Board of Health and president of the American Public Health Association in 1937, died in Louisville, August 7, aged 70, of coronary sclerosis. His death brought to an end a career of more than forty-five years in public medical service. Dr. McCormack was born in Nelson County, Ky., Aug. 21, 1872. He was the son of Dr. Joseph Nathaniel McCormack, renowned as one of the most important leaders in the reorganization and building of the American Medical Association. Following graduation from Ogden College at Bowling Green, Ky., where he received the B.A. degree in 1892, he attended the College of Physicians and Surgeons of Columbia University and received his M.D. degree in 1896. He then returned to Kentucky, opened an office in Bowling Green in 1897 and soon thereafter was named health officer of Warren County. He became assistant state health officer in 1898 and held that position until 1912, when he became state health commissioner.

In 1900 Dr. McCormack became surgeon general of the Kentucky National Guard and held that position until 1908. In 1911 he accepted a commission as lieutenant in the Medical Reserve Corps. With the beginning of World War I in 1917 he was appointed major and organized Base Hospital No. 59. He was about to proceed overseas with the base hospital when he was ordered to the Panama Canal Zone by General Gorgas, succeeding General Gorgas as chief health officer and completing the building of the Ancon Hospital. In this position he held the rank of lieutenant colonel. An interesting feature of that service was his control of an epidemic of cerebrospinal meningitis on the Japanese S. S. *Anyo Maru*. For this he received the special thanks of the mikado. He was a member of the Association of Military Surgeons and secretary and president of the Medical Veterans of the World War.

ARTHUR THOMAS MCCORMACK, M.D., 1872-1943

In all work in the field of public health in America Dr. McCormack was prominent. His death concluded more than thirty years as secretary of the Kentucky State Board of Health. He had been president of the American Public Health Association in 1937, special consultant of the U. S. Public Health Service, and organizer and dean of the School of Public Health of Kentucky. He had been president of the Conference of State and Provincial Health Authorities of North America, and he was a member of the National Tuberculosis Association, Gorgas Memorial Institute and the National Health Council. His most important recent activity was the presentation of a report on the establishment of full time county health departments, published in THE JOURNAL. In his public life Dr. McCormack had been president of the Kentucky Conference on Social Work, and he was state flood director for the flood which menaced Kentucky in 1937.

In the field of organized medicine Dr. McCormack was prominent as secretary of the Kentucky State Medical Association for many years. He founded the *Kentucky Medical Journal* in 1901 and was subsequently director and editor. He was a fellow of the American College of Surgeons and of the American Medical Association. He served in the House of Delegates from 1908 to 1914, 1916-1917, 1919 to 1931, in 1935 and again from 1937 to 1943 inclusive. During these years he gave of his time and thought on many occasions to the many reference committees to which he was assigned and in which he was especially efficient because of his many years of service. He was president-elect of the Southern Medical Association in 1939 and president in 1940. During recent years he had spent much time in Washington acting in an advisory capacity to several government agencies. For his work in the field of public health and education he was honored with the M.A. from Bethel College at Russellville, Ky., in 1900, the degree of Dr.P.H. from Detroit College of Medicine and Surgery in 1925, the degree of D.Sc. from Berea (Ky.) College in 1926, and LL.D. from Transylvania University in 1930. The literary contributions of Dr. McCormack included many editorials and articles for the journal which he edited. He wrote also a book entitled "Course in Physical Education for the Common Schools of Kentucky," published in 1920. His heredity, statesmanship, idealism and devotion to the public good and to public service made Dr. McCormack a notable figure in American medicine.

Charles Macfie Campbell ✠ noted psychiatrist, died at Wyman House, Cambridge, Mass., August 7, of heart disease, aged 66.

Born in Edinburgh, Scotland, Sept. 8, 1876, Dr. Campbell studied at George Watson's College, receiving the M.A. at Edinburgh University in 1897, the M.B. and Ch.B. in 1902 and the degree of doctor of medicine in 1911. He came to the United States in 1904 and became a citizen in 1918. For a time he was assistant physician at the Psychiatric Institute at Ward's Island, New York, and at Bloomingdale Hospital, White Plains. In 1913, following several years as instructor in psychopathology at Cornell University Medical College, Dr. Campbell went to Johns Hopkins University School of Medicine to become associate professor of psychiatry and associate psychiatrist at the Johns Hopkins Hospital and to serve under the direction of Adolf Meyer in the newly opened Phipps Psychiatric Institute. In 1920 he joined the Harvard Medical School as professor of psychiatry, later assuming the position of medical director of the Boston Psychopathic Hospital.

Dr. Campbell was a sponsor of the early movement to establish an organized program of mental hygiene in this country. Long identified with the National Committee for Mental Hygiene, he was in 1931 named one of a group to serve as an advisory board to its new division of psychiatric education. In 1932 he returned to his native land to participate in the one hundredth anniversary of the British Medical Association.

Dr. Campbell served as president and vice president of the American Board of Psychiatry and Neurology, Inc., and president of the American Psychiatric Association, Massachusetts Society for Mental Hygiene and Massachusetts Psychiatric Society. He was a member of the Association for Research in Nervous and Mental Disease, once serving as vice president, the American Neurological Association, New England Society of Psychiatry, American Psychopathological Association, American School Hygiene Association, British Medical Association, Royal Medico-Psychological Association of Great Britain and Ireland and the Royal Society of Medicine of England. He delivered such notable lectures as the Thomas W. Salmon Memorial, Gehrmann, Pasteur and Lowell lectures. In addition to numerous articles, Dr. Campbell was the author of "Destiny and Disease in Mental Disorders," "Delusion and Belief," "Focal Symptoms in General Paralysis," "Human Personality and the Environment," "A Present-Day Conception of Mental Disorders" and "Towards Mental Health: The Schizophrenic Problem."

William Henry Humiston, Vero Beach, Fla.; Long Island College Hospital, Brooklyn, 1879; member of the House of Delegates of the American Medical Association in 1902; member and past president of the Ohio State Medical Association; past president of the Cleveland Medical Society and the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; clinical professor emeritus of gynecology at the Western Reserve University School of Medicine; for six years a member of the board of health of Cleveland; a member of the original Troop A, 107th Cavalry of the Ohio National

Guard; during World War I served as a member of the district board of appeals; formerly a director of the Cleveland Chamber of Commerce; formerly gynecologist on the staff of the City Hospital, Cleveland; for many years on the staff of St. Vincent Charity Hospital, Cleveland, where he died. June 15, of myocarditis, aged 87.

Bert Raymond Hoobler, Detroit; Cornell University Medical College, New York, 1905; member of the Michigan State Medical Society and the American Pediatric Society; emeritus professor of pediatrics at the Wayne University College of Medicine, where he had been professor and head of the department from 1914 to 1936; at one time on the staff of the Bellevue Hospital, New York; organizer and medical superintendent of the Hoobler Convalescent Hospital and Rest Home; served as chief of the medical staff of the Children's Hospital; a member of the staffs of the Woman's Hospital, Harper Hospital, Florence Crittenton Hospital, William Booth Memorial Hospital, Receiving Hospital and the Harper Hospital, where he died, June 11, of coronary thrombosis, aged 71.

Walter Douglas Bishop, Kansas City, Kan.; Atlanta Medical College, 1915; member of the Kansas Medical Society; for five years Wyandotte county physician; served during World War I; member of the staffs of the Providence, Bethany and St. Margaret's hospitals; aged 56; died, May 21, of coronary occlusion.

Wilbur Howard Bliss, Northboro, Mass.; Long Island College Hospital, Brooklyn, 1889; aged 84; died, April 25, of carcinoma of the prostate.

Otis J. Bryan ✠ Pecos, Texas; Memphis (Tenn.) Hospital Medical College, 1902; past president and secretary of the Reeves-Ward-Winkler-Pecos Counties Medical Society; chairman of the Selective Service Board for Reeves County during World War I and recently; for fifteen years served as health officer of Reeves County; member of the school board; aged 63; died, April 28.

Louis Leonard Corcoran ✠ Rock Rapids, Iowa; Northwestern University Medical School, Chicago, 1907; aged 66; died, May 18.

Frank Eastman, Atlanta, Ga.; Hahnemann Medical College of Philadelphia, 1877; aged 87; died, June 8, in St. Joseph's Infirmary of chronic myocarditis.

Hans Edward Eiel ✠ Buffalo Center, Iowa; Keokuk (Iowa) Medical College, 1899; past president and secretary of the Hancock-Winnebago Counties Medical Society; formerly health officer; postmaster of Buffalo Center; aged 67; died, May 29, in the Dolmage Hospital of coronary thrombosis.

Erle D. Forrest, Cranston, R. I.; Tufts College Medical School, Boston, 1912; aged 54; died, May 25, in the Jane Brown Memorial Hospital, Providence, of hypertensive cardiovascular disease.

William H. Gohlman, Van Nuys, Calif.; Medical Department of Tulane University of Louisiana, New Orleans, 1896; aged 69; died, May 17, of cerebral hemorrhage and hypertension.

John C. Gourley ✠ Windber, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1904; a member of the board of education of Windber from 1924 to 1930; roentgenologist and obstetrician to the Windber Hospital; aged 68; died, May 16, of cerebral arteriosclerosis.

Edward Benjamin Gray, Cincinnati; Howard University College of Medicine, Washington, D. C., 1913; served during World War I; aged 55; died, May 27, in the Jewish Hospital.

John Louis Gray ✠ Anderson, S. C.; Bellevue Hospital Medical College, New York, 1895; served on the staff of the Anderson County Hospital; aged 74; died, May 19, of heart disease.

Ernest Nelson Greenman ✠ Kankakee, Ill.; Jefferson Medical College of Philadelphia, 1912; served during World War I; aged 56; died May 31, of heart disease.

Ezra Clarence Grim ✠ Kirksville, Mo.; Washington University School of Medicine, St. Louis, 1901; an Affiliate Fellow of the American Medical Association; the founder and formerly superintendent of the Grim-Smith Hospital and Clinic; aged 69; died, May 26, of uremia.

Augustus G. Haerther, Chicago; Chicago Medical College, 1883; aged 88; died, May 30, of intestinal obstruction and carcinoma of the hepatic flexure of the colon.

George P. Hale, Memphis, Mich.; the Hahnemann Medical College and Hospital, Chicago, 1887; for many years health officer; aged 86; died, May 21, of heart disease.

William Wilson Hale, Cheyenne, Wyo.; College of Physicians and Surgeons, Keokuk, Iowa, 1877; at one time professor of therapeutics at the Drake University College of Medicine, Des Moines; aged 91; died, May 24, in the Memorial Hospital of Laramie County of chronic glomerulonephritis.

John Mead Hall ✠ New York; Cornell University Medical College, New York, 1904; formerly deputy health officer of the Port of New York; served in the medical corps of the U. S. Army during World War I; on the staff of the New York Eye and Ear Infirmary as senior assistant surgeon until February 1943, when he retired as an honorary surgeon; aged 62; died, June 7, in the New York Hospital of heart block.

Guido B. Hammond, English, Ind.; Kentucky School of Medicine, Louisville, 1903; member of the Indiana State Medical Association; for many years president of the school board; president of the English State Bank and the Crawford County Security Company; aged 67; died, June 7, in the Kentucky Baptist Hospital, Louisville, of hemorrhage following a gastroenterostomy.

Robert Thomas Hawks, Carson, Va.; Medical College of Virginia, Richmond, 1907; chairman of the school board and coroner of Prince George County for many years; medical examiner for the Prince George Selective Service Board; a director of the Bank of Southside Virginia; aged 60; died, June 8, of angina pectoris.

William F. Hilger, Milwaukee; Milwaukee Medical College, 1903; also a pharmacist; aged 69; died, May 22, in St. Anthony Hospital of coronary occlusion.

Emma Linton Hill ✠ Oswego, Kan.; Kansas Medical College, Topeka, 1895; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; aged 84; died, May 14, in the Mercy Hospital, Parsons, of injuries received in an automobile accident.

L. L. Hines, Richland Center, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1909; on the staff of the Richland Hospital; aged 71; died, May 21, of nephritis.

Francis Victor Hoehn ✠ Buffalo; University of Buffalo School of Medicine, 1910; served as a captain in the medical corps of the U. S. Army in France during World War I; a member and vice president of the medical staff of the Charity Eye, Ear and Throat Hospital of Erie County; consulting rhinolaryngologist to the Edward J. Meyer Memorial Hospital; member of the staffs of St. Mary's Infant Asylum and Maternity Hospital and the Emergency Hospital of the Sisters of Charity, where he died, June 1, of ischiorectal abscess, aged 64.

Jacob J. Hood ✠ Cicero, Ill.; Jenner Medical College, Chicago, 1902; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; for seven years health commissioner of Cicero; one of the founders and directors of the Cicero State Bank; on the staff of the Garfield Hospital, Chicago; aged 73; died, May 27, of intestinal obstruction.

Frank Ignatius Horn, Los Angeles, Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1894; member of the California Medical Association; aged 73; on the visiting staff of the Cedars of Lebanon Hospital, where he died in May of hypertrophy of the prostate and septicemia.

Edward Hougen ✠ Wisconsin Rapids, Wis.; Northwestern University Medical School, Chicago, 1897; aged 72; died, June 21, in the Memorial Hospital, Sheboygan, of epithelioma of the tongue.

John Blanch Howell ✠ Canton, Miss.; Vanderbilt University School of Medicine, Nashville, Tenn., 1905; president of the Central Medical Society in 1933; member of the Mississippi State Board of Health from 1936 to 1942; chief surgeon on the staff of the Kings Daughters Hospital; surgeon for the Illinois Central Railroad; formerly a captain of the Mississippi National Guard; physician-surgeon for the Pearl River Lumber Company; past president of the Rotary Club; aged 62; died, May 24, of coronary occlusion.

Francis Eugene Hubbard, Eau Claire, Mich.; Michigan College of Medicine and Surgery, Detroit, 1902; for many years a druggist; served several terms on the school board; aged 77; died, June 17, of carcinoma.

Percy Hudson, Utica, Miss.; Louisville (Ky.) Medical College, 1906; member of the Mississippi State Medical Association; aged 60; died, May 27, of heart disease.

Julius Kershaw Huff, Hodges, S. C.; Jefferson Medical College of Philadelphia, 1894; aged 70; died, June 6, of malignant tumor of the esophagus.

Alonzo Homer Kenniebrew, Springfield, Ill.; Meharry Medical College, Nashville, Tenn., 1897; aged 68; died, May 20, in St. John's Hospital of hypertensive heart disease and bronchopneumonia.

Allan Napier Kerr, Pacific Palisades, Calif.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1903; member of the Washington State Medical Association; for many years on the staffs of various Veterans Administration facilities; aged 68; died, May 6, in the Veterans Administration Facility, West Los Angeles, of granuloma of the septum and pulmonary edema.

Edward R. Layne, Whittier, Calif.; Arkansas Industrial University Medical Department, Little Rock, 1888; aged 86; died, May 25, of coronary thrombosis and arteriosclerosis.

Arthur Jack Leader, Poughkeepsie, N. Y.; Syracuse University College of Medicine, 1930; member of the Medical Society of the State of New York and the American Psychiatric Association; senior assistant physician to the Hudson River State Hospital; aged 35; died, May 31, of carcinomatosis and mediastinal chondromyxosarcoma.

Max David Mayer ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1915; specialist certified by the American Board of Obstetrics and Gynecology, Inc.; member of the American Psychoanalytic Association; fellow of the American College of Surgeons; on the staffs of Mount Sinai and Sydenham hospitals and New York Home for Aged and Infirm Hebrews; aged 50; died, May 28, of leukemia.

William C. McCammon, Knoxville, Tenn.; Tennessee Medical College, Knoxville, 1899; aged 71; died, June 3, of carcinoma of the stomach.

Henry C. McQuillin, Madison, Wis.; Physio-Medical College of Indiana, Indianapolis, 1897; aged 70; died, May 25, of hypertensive cardiovascular renal disease.

Nelson Merrill ✠ Marshalltown, Iowa; State University of Iowa College of Medicine, Iowa City, 1893; served one term as a member of the Marshalltown independent school district; on the staffs of the Evangelical Deaconess Home and Hospital and St. Thomas Mercy Hospital; aged 80; died, May 21, of angina pectoris.

Charles S. Newlon ✠ Kansas City, Mo.; College of Physicians and Surgeons, Keokuk, Iowa, 1881; an Affiliate Fellow of the American Medical Association; at one time superintendent of the School for Feeble-Minded Youth, Winfield, Kan.; aged 85; died, June 4, of carcinoma of the liver.

LIEUT. COL. SIMON WARMENHOVEN
1910-1943, M. C., U. S. ARMY

William Boyd Nicholl, Oakland, Calif.; Colorado School of Medicine, Boulder, 1901; aged 69; died, April 8, of coronary thrombosis and hypertension.

Sofie Amalia Nordhoff-Jung ✠ Washington, D. C.; Columbian University Medical Department, Washington, 1893; professor of gynecology emeritus at the Georgetown University School of Medicine; in 1923 established the Sofie A. Nordhoff-Jung Cancer Research Prize to encourage researches in the etiology, prevention and treatment of cancer; in 1927 received a medal from the German government for distinguished services in Red Cross work rendered in Germany before the United States entered World War I; aged 76; died, June 6.

John Eugene Osborne, Rawlins, Wyo.; University of Vermont College of Medicine, Burlington, 1880; formerly governor of the state of Wyoming and mayor of Rawlins; in 1896 elected representative to Congress; at one time first assistant secretary of state; chairman of the board of directors and for many years president of the Rawlins National Bank; aged 89; died, April 24, of chronic myocarditis.

Eleanor Parry ✠ Huntington, N. Y.; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1894; aged 82; died, May 22, in the New York Infirmary for Women and Children, New York.

Felix Peebles, Jefferson, Texas; Gate City Medical College, Texarkana, Ark., 1905; St. Louis College of Physicians and Surgeons, 1913; member of the State Medical Association of Texas; past president and secretary of the Cass-Marion Counties Medical Society; examiner for the Selective Service of Marion County; aged 63; died, April 5, of cerebral hemorrhage and myocarditis.

Robert Sheild Perkins, Norfolk, Va.; Hahnemann Medical College of Philadelphia, 1872; aged 95; died, June 4, of heart disease.

Henry Lincoln Plummer, Boston; Harvard Medical School, Boston, 1890; aged 75; died, May 25, in the Boston City Hospital.

Jacob H. Polozker, Detroit; Detroit College of Medicine, 1910; served on the staff of the Children's Hospital; aged 55; died, May 15, of coronary thrombosis.

William Fletcher Priestley, Oakland, Calif.; Cooper Medical College, San Francisco, 1912; member of the California Medical Association; served during World War I; at one time health officer of San Joaquin County; aged 58; died, May 29, of coronary thrombosis.

James Pullman ✠ Brooklyn; Yale University School of Medicine, New Haven, Conn., 1899; formerly clinical professor of medicine at the Long Island College of Medicine; served on the staffs of the Kings County, Lutheran and Swedish hospitals; aged 68; died, May 28, of arteriosclerotic heart disease.

Samuel Henry Watters, Iowa City, Iowa; University of the City of New York Medical Department, 1884; aged 91; died, May 30, of senility.

William R. Wellborn, Elkin, N. C.; North Carolina Medical College, Davidson, 1905; a member of the staff of Hugh Chatham Memorial Hospital; aged 60; died suddenly, May 24, of coronary occlusion.

Edward Hayward Wells ✠ New York; Bellevue Hospital Medical College, New York, 1895; aged 77; died, May 18, of angina pectoris.

James S. Wheeler, Greer, S. C.; University of Nashville (Tenn.) Medical Department, 1902; formerly a member of the U. S. Public Health Service Reserve; veteran of the Spanish-American War and World War I; aged 70; died, May 28, in the Greenville (S. C.) General Hospital.

Warren Everett White, Spokane, Wash.; Kansas City (Mo.) Medical College, 1902; aged 69; died, May 25, of cardiovascular renal disease.

Samuel Sherman Widener, Pondcreek, Okla.; Chattanooga (Tenn.) Medical College, 1903; veteran of the Spanish-American War; aged 68; died, May 8, of cerebral hemorrhage.

James Griffin Wilbanks, Amarillo, Texas; Birmingham (Ala.) Medical College, 1912; member of the State Medical Association of Texas; on the staffs of the Northwest Texas Hospital and St. Anthony's Hospital; aged 60; died, May 27, of coronary thrombosis.

Thomas Robert Waters Wilson ✠ Greenville, S. C.; Baltimore Medical College, 1897; past president and secretary of the Greenville County Medical Society; served in the medical corps of the U. S. Army during World War I; aged 68; for twenty-eight years pathologist at the Greenville General Hospital, where he died, May 3, of cerebral arteriosclerosis and left hemiplegia.

Isaac Henry Wineberg ✠ Quincy, Ill.; Chicago Medical School, 1927; served on the staffs of St. Mary and Blessing hospitals; aged 54; died, May 12, of coronary occlusion.

Abraham Samuel Wingersky, Boston (licensed in Massachusetts in 1898); aged 67; died in May.

KILLED IN ACTION

Simon Warmenhoven, Grand Rapids, Mich.; Marquette University School of Medicine, Milwaukee, 1939; began active duty in October 1940 as a captain in the medical corps of the U. S. Army (National Guard) attached to the 126th Infantry Medical Detachment at Camp Livingston, La., and later became a major and lieutenant colonel; aged 33; was killed in action in the Southwest Pacific, May 5.

Correspondence

SALT REQUIREMENTS IN HOT CLIMATES

To the Editor:—I was attracted by the letter in THE JOURNAL, July 24, from the London correspondent in regard to "Salt and Water Requirements in Hot Climates." Take the figures quoted from the Army Medical Department bulletin that in hot countries a man on exercise excretes from 5 to 8 liters of sweat and needs not over 25 Gm. salt unless the sweat exceeds 2 gallons (Imperial measure, I presume) or a little over 9.5 liters. Sweat is hypotonic. Consequently when a liter is excreted there would be but for the kidney a hypertonic condition in the intracellular fluids. The kidney, however, guards the salt concentration zealously and excretes sufficient salt to keep the fluids isotonic. The net result of losing a liter of sweat is that of losing a liter of isotonic solution containing 8.5 Gm. of salt. If a man is to lose but 5 liters of sweat it means he has lost 42.5 Gm. of salt. If this keeps up a man is bound to get out of balance and get miners' cramps. The article states that for hard work more than 9 liters is required, to be supplemented by salt tablets to be taken during meals or rest periods. The tablets are of 10 Gm., taken with a pint of water. It would be more rational to take these at more frequent intervals.

RODGER J. B. HIBBARD, M.D., State Sanatorium, Ark.

CHEMOSURGERY AND RADIATION THERAPY IN EXTERNAL CANCER

To the Editor:—I do not wish to let go unchallenged the partial misconception held by your editorial writers regarding the relative efficiency of chemosurgery and radiation therapy in the treatment of external cancer. Those of us who have had the opportunity of seeing hundreds of cancers respond to chemosurgery after previous unsuccessful x-ray or radium treatment know that, despite the modern physical perfection of these agents, they can never approach the effectiveness of chemosurgery.

Tumors vary greatly in radiosensitivity, and for this reason a great many do not respond even to the most expert radiation therapy. Moreover, the radiotherapist has no way of knowing the exact extent of a carcinoma except perhaps in its earliest stages. Our reconstructions of carcinomas frequently show small caliber outgrowths which had been completely unsuspected from clinical examination; these can be accurately followed out and eradicated by the chemosurgeon, but the radiotherapist would never know they were there, though he might suspect it when recurrences appeared months or years later.

It is natural that some of those particularly interested in radiation therapy will be loath to admit the value of competing methods; thus Ackerman and Eberhard apparently were not convinced of the superiority of chemosurgery except in certain cancers no longer amenable to radiation or surgery. It is my contention that the microscopic control afforded by chemosurgery is also very advantageous in the treatment of early cancer. Dr. Ackerman visited me after clinic hours for a hurried fifteen minute talk, and it is probable that he did not get a complete insight into all the applications of chemosurgery. I gave him my complete approval in his fight against irregular cancer paste practitioners as long as he didn't confuse the University of Wisconsin's chemosurgery with them. Incidentally, he has since asked me to treat a patient whose cancer did not respond to radiation therapy in his institution.

I only ask that the profession keep an open mind on the subject until I am able to muster the data which will eventually prove the worth of chemosurgery. Unfortunately time is required, so, although the series now amounts to 1,200 cases, those treated three and five years ago are only now reaching satisfactory numbers.

FREDERIC E. MOHS, M.D., Madison, Wis.
Assistant Professor of Chemosurgery, State of Wisconsin General Hospital.

USE OF POWDERED SULFATHIAZOLE IN NOSE AND THROAT

To the Editor:—In THE JOURNAL of May 15 under Current Comment, page 180, I read of the use of sulfathiazole locally in the nasopharynx and larynx, using a finely powdered spray blown into the nostrils, pharynx and larynx, or using a solution in ¼ cup of hot water of a 7½0 grain (0.5 Gm.) tablet of sulfathiazole as a gargle, as reported by Fenton and Freeman.

For the past two years I have used 7½0 grains to 15 grains of sulfathiazole in ¼ cup of hot water as a gargle, but, better yet, have both my patients and myself chew a stick of chewing gum and then wrap a 7½0 grain tablet of sulfathiazole in the gum mass and chew the mixture and keep it in the mouth as long as possible. The taste is slightly bitter at first but then rapidly becomes sweet. Immediate relief of pain and discomfort in the throat invariably follows.

I have thought of incorporating a tablet of sulfathiazole in flavored hard candy to be used as a lozenge and believe this could be beneficial in throat infections, especially for children.

By means of the chewing gum method, I believe the concentration of sulfathiazole can be maintained in the mouth and pharynx for some time, since the solubility of the drug is constant. It is well known that gargles do not reach the nasopharynx, while swallowed saliva does. I have used this method during the day as frequently as I believed necessary.

It has been interesting and enjoyable to me to be able to read of procedures used by individuals who thought along similar lines at almost the same time as others.

JOSEPH GERTNER, Lieutenant, M. C., A. U. S.

SWELLING OF POPLITEAL BURSAE IN BRUCELLOSIS

To the Editor: The article by Meyerding and Van Demark on "Posterior Hernia of the Knee" in the July 24 issue of THE JOURNAL impels me to call attention to the fact that swelling of popliteal bursae may also be associated with such systemic illnesses as chronic brucellosis.

In this infection, about which too little is known, I have observed six instances of popliteal bursitis of varying size and accompanied by from little to rather considerable discomfort. In all cases but 1 there was either pronounced improvement or disappearance of the bursal involvement when these patients responded clinically and serologically to Brucella abortus vaccine treatment. Since none were treated surgically it is impossible to say whether any cases represented true hernia of the synovial lining of the knee joint or whether they were all noncommunicating bursae.

There is no reference in the literature to popliteal bursitis in brucellosis as far as I have been able to determine. I briefly mentioned it in my monograph "Brucellosis (Undulant Fever) Clinical and Subclinical."

HAROLD J. HARRIS, Lieutenant Commander (MC), U. S. N. R.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, Aug. 14, page 1125.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 20-22. Sec., Dr. B. F. Austin, 519 Dexter Ave., Montgomery.

ARKANSAS: * *Medical.* Nov. 3-4. Sec., Dr. D. L. Owens, Harrison. *Eclectic.* Little Rock, Nov. 4. Sec., C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Written.* Sacramento, Oct. 18-21. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento.

DISTRICT OF COLUMBIA: * Washington, Nov. 8-9. Sec., Commission on Licensure, Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington.

FLORIDA: * Jacksonville, Nov. 22-23. Sec., Dr. William M. Rowlett, Box 786, Tampa.

ILLINOIS: Chicago, Oct. 12-14. Superintendent of Registration, Department of Registration and Education, Mr. Philip M. Harman, Springfield.

INDIANA, Indianapolis, Sept. 14-16. Sec., Board of Medical Registration & Examination, Dr. W. C. Moore, 301 State House, Indianapolis.

IOWA: * Iowa City, Dec. 27-29. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

KANSAS: Topeka, Dec. 14-15. Sec., Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

KENTUCKY: Louisville, Dec. 6-8. Sec., Dr. A. T. McCormack, 620 S. Third St., Louisville.

MARYLAND: *Medical.* Baltimore, Dec. 14-17. Sec., Dr. J. T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, Dec. 14-15. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MICHIGAN: * Ann Arbor, Oct. 13-15. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

MINNESOTA: * Minneapolis, Oct. 19-21. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul.

MISSISSIPPI: Jackson, September. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: Helena, Oct. 5-6. Sec., Dr. O. G. Klein, First Nat'l Bank Bldg., Helena.

NEW HAMPSHIRE: Concord, Sept. 9-10. Sec., Board of Registration in Medicine, Dr. D. G. Smith, State House, Concord.

NEW JERSEY: Trenton, Oct. 19-20. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * *Endorsement.* Santa Fe, Oct. 11-12. Sec., Dr. LeGrand Ward, 141 Palace Ave., Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Sept. 20-23. Sec., Dr. R. R. Hannon, Education Bldg., Albany.

OHIO: *Endorsement.* Columbus, Oct. 7. *Written.* Columbus, Dec. 4. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

SOUTH CAROLINA: Charleston, Dec. 20-22. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

VERMONT: Burlington, Dec. 15-17. Sec., Dr. F. J. Lawliss, Richford.

VIRGINIA: Richmond, Dec. 14-17. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WYOMING: Oct. 4-5. Sec., Dr. M. C. Keith, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Tucson, Sept. 21. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson.

COLORADO: Denver, Sept. 8-9. Sec., Dr. E. B. Starks, 1459 Ogden St., Denver.

CONNECTICUT: Oct. 9. Address State Board of Healing Arts, 250 Church St., New Haven.

DISTRICT OF COLUMBIA: Washington, Oct. 18-19. Sec., Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington.

FLORIDA: DeLand, Nov. 6. Sec., Dr. John F. Conn, John B. Stetson University, DeLand.

IOWA: Des Moines, Oct. 12. Dir., Division of Licensure & Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MINNESOTA: Minneapolis, Oct. 5-6. Sec., Dr. J. C. McKinley, 126 Millard Hall, Univ. of Minnesota, Minneapolis.

NEBRASKA: Lincoln, Oct. 5-6. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln.

OREGON: Portland, Oct. 30. Sec., State Board of Higher Education, Mr. C. D. Byrne, University of Oregon, Eugene.

SOUTH DAKOTA: Vermillion, December. Sec., Dr. G. M. Evans, Yankton.

WISCONSIN: Madison, Sept. 18. Sec., Prof. R. N. Bauer, 152 W. Wisconsin Ave., Milwaukee.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Osteopathic Practice Acts (California): Power of Legislature to Impose Educational Standards in Addition to Those Imposed in the Osteopathic Initiative Act of 1922.—Under the applicable California law between 1913 and 1922 all persons, whether they were nonsectarian practitioners, homeopaths, eclectics or osteopaths, desiring licenses to practice the healing art without restriction and possessing the qualifications prescribed by law, were examined and licensed by the board of medical examiners. A separate osteopathic practice act in the form of an initiative measure was adopted by the California electorate in 1922, which created an independent board of osteopathic examiners and gave "it jurisdiction, formerly residing in the Board of Medical Examiners, over graduates of osteopathic schools." The initiative measure "was intended to effect administrative changes only and made no substantive changes in the standards of education and examination for the physician and surgeon certificate" [the license to practice without restriction] required under the existing medical practice act. In the words of the court, the initiative made "the Medical Practice Act [presumably the educational requirements therein] applicable to graduates of osteopathic schools." Subsequently a so-called business and professions code (a codification of the then existing statutory provisions relating to the licensing of businesses, professions and vocations) was adopted by the legislature and by an amendment to that code enacted in 1941 it was provided that before a previously licensed osteopath could effect an annual registration, which would give him the legal right to practice during the ensuing year, he must, in addition to paying the required annual license fee, present evidence that in the preceding year he had completed a minimum of thirty hours of professional educational work approved by the osteopathic board.

The petitioner, a graduate of an osteopathic school, who was issued a physician and surgeon certificate (the license issued permitting the practice of medicine and surgery without restriction) by the osteopathic board in 1934, refused to tender for the issuance of an annual registration certificate for 1943 "evidence of the performance of thirty hours of professional educational work" during 1942. When the osteopathic board refused to issue to him the certificate desired he brought mandamus to the Supreme Court of California to compel the board to do so.

The osteopath contended, first, that since the osteopathic initiative act adopted in 1922 "made the Medical Practice Act [presumably the education requirements contained therein] applicable to graduates of osteopathic schools such rights and duties remain invariable." Apparently the gist of this contention was that since the osteopathic initiative act was adopted by the electorate it could be amended in no particular by the legislature and that since the initiative adopted the educational standards imposed by the then existing medical practice act the provision adopted by the legislature in amending the business and professions code in 1941 requiring osteopaths annually to complete a minimum of thirty hours of professional educational work was an invalid attempt to amend the initiative act of 1922. There is no provision in the osteopathic initiative act, answered the Supreme Court, limiting the power of the legislature to change the standards for receiving or holding a physician and surgeon certificate. The argument submitted to the voters in 1922 in support of the initiative act set forth that that act left the legislature free to change the standards of education and examination. The initiative act itself demonstrates the care with which its framers guarded that freedom and made the act exclusively administrative in character, clearly leaving it to future legislatures, as they saw fit, to impose additional educational requirements on osteopaths.

The osteopath next contended that the 1941 amendment to the business and professions code violates article I, section 21

of the constitution of California in that, since osteopaths must meet the same educational requirements as other practitioners who are legally entitled to practice medicine and surgery without restriction, they cannot be subjected to requirements in addition to those imposed on the others and that no practitioners other than osteopaths are required to complete thirty hours of professional educational work during any one year. It is generally recognized, however, said the Supreme Court, that the power to regulate the treatment of disease is an elastic one and that regulations may vary according to the schools or methods of practice as long as they entail no unreasonable discrimination, citing *In re Rust,* 181 Cal. 73, 183 P. 548, which held the California optometry act of 1913, forbidding osteopaths but not nonsectarian physicians from practicing optometry without a license from the state board of optometry, did not violate article I, section 21 of the state constitution. The opinion in that case, continued the court, set forth a history of the distinctions that the legislature has made at various times between practitioners of osteopathy and other practitioners. Thus for many years different licenses were issued to osteopaths than to physicians and surgeons with different rights and duties attached to the respective licenses. Although the certificates as well as the educational requirements for osteopaths and physicians and surgeons may now be the same, the legislature is as free to return to different certificates and educational requirements as it was to abandon them. The petition for writ of mandate was denied.—*Gamble v. Board of Osteopathic Examiners of California,* 130 P. (2d) 382 (Calif., 1942).

Charitable Hospitals: Liability for Failure to Furnish Proper Equipment.—Mrs. Canney was received about 9:30 p. m., Nov. 7, 1940, as a pay patient in the Providence hospital, a charitable institution, to be delivered of child. A cesarean section was performed on her about an hour later, after which she was given a blood transfusion and taken to her room about 11:50 p. m. She was placed in a bed previously heated with an electric pad which had been removed. The patient was left in charge of a special nurse, obtained for the patient by the hospital at her husband's request, and this nurse was alone with the patient from 1 to 7 a. m. About 5 or 6 a. m. when the nurse bathed the patient it was discovered that both heels were burned. What heating appliances, if any, had been placed in the bed by the special nurse between midnight and that time are not shown, since the nurse was not called as a witness in the litigation that subsequently ensued. Later the patient and her husband brought suit against the hospital, alleging that the patient's injuries

> were the sole, direct and proximate result of the administrative negligence of the defendants, which consisted solely of the failure of defendants to furnish proper equipment for the purpose of warming the feet of plaintiff under a regulated heat so that the said application of the said instrument would not result in injury . . .

From a judgment in favor of the plaintiffs, rendered on a verdict of the jury, the hospital appealed to the Supreme Court of Washington.

The defendant hospital, said the Supreme Court, being a charitable hospital, is not liable for the negligent act of an employee, unless it is established that the hospital failed to exercise ordinary care in the selection or retention of the negligent employee. The fact that compensation is exacted for services rendered does not, of itself, deprive an institution of its charitable status. It is generally held that, since a special nurse is the agent of the patient and is not an employee of the hospital and not subject to its control, the acts of the special nurse do not create liability on the part of the hospital. The plaintiffs invoke the rule enunciated in *Miller* v. *Sisters of St. Francis,* 5 Wash. (2d) 204, 105 P. (2d) 32, that a hospital, even if it is a charitable institution, will be required to respond in damages for injuries proximately resulting from failure to furnish proper equipment, which failure apparently would constitute "what is called administrative negligence as distinct from failure to exercise due care in the selection of proper physicians and nurses." That rule, however, continued the court, is subject to the qualification that if the article which it is the duty of the hospital to supply is obviously unfit for the use for which it was intended, and a special nurse in charge of a patient uses it in violation of the standards of care of nursing practice, the hospital cannot be chargeable with any injurious effects therefrom but the rule is otherwise if the defect is not patent. See *Payne* v. *Santa Barbara Cottage Hospital,* 2 Cal. App. (2d) 270, 37 P. (2d) 1061 and *Ratliffe* v. *Wesley Hospital,* 135 Kan. 306, 10 P. (2d) 859. If we apply the law to the facts of this case, it is clear that the trial court was not warranted in submitting the cause to the jury for its determination as to the negligence of the hospital. From midnight, when she was returned from the operating room to her private room, until 7 a. m., the patient was in charge of a special nurse who had been employed at the request of her husband. The special nurse was not called as a witness. What heating appliances, if any, she placed in the patient's bed during the period she was in charge of the patient are not known. There is an absence of evidence of any lack of care on the part of the hospital in providing competent servants. There is no evidence that the hospital failed to furnish proper appliances. The mother of the patient testified that between 9:30 and 10 a. m., about five hours subsequent to the time it was discovered that the patient had burns on her feet, she called to see the patient and saw an ordinary rubber hot water bottle which, although it was not hot then, was at the patient's feet. She testified that she could not tell whether there was any cover on the hot water bottle. On the other hand, evidence was adduced on behalf of the hospital that the hot water bottles supplied by it are standard equipment used in all hospitals; that covers are supplied for the hot water bottles, which are never used without a cover, and that a hot water bottle is always placed between the blankets and never next to the patient. If, said the court, the special nurse placed an uncovered hot water bottle to the feet of the patient, that failure of the special nurse in not having the bottle covered or in protecting it by blankets is not administrative negligence on the part of the hospital. If the hot water bottle supplied by the hospital was obviously unfit for the use for which it was intended—and there is no showing to that effect in the record—and if the special nurse who was employed by and was the agent of the patient and her husband used it in violation of the usual standards of nursing practice, the hospital cannot be charged with the resultant injurious effects on the patient.

The judgment in favor of the patient and her husband was accordingly reversed and the cause remanded with direction to dismiss the action.—*Canney v. Sisters of Charity of House of Providence, 130 P. (2d) 899 (Wash., 1942).*

Society Proceedings

COMING MEETINGS

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 9-11. Dr. James R. Bloss, 418 Eleventh St., Huntington, W. Va., Secretary.

American Congress of Physical Therapy, Chicago, Sept. 8-11. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.

District of Columbia, Medical Society of the, Washington, Sept. 30-Oct. 2. Mr. Theodre Wiprud, 1718 M St. N.W., Washington, Secretary.

Indiana State Medical Association, Indianapolis, Sept. 28-30. Mr. T. A. Hendricks, 23 East Ohio St., Indianapolis, Executive Secretary.

Kansas City Southwest Clinical Society, Kansas City, Mo., Oct. 4-6. Dr. William M. Korth, 1115 Grand Ave., Kansas City, Mo., Secretary.

Kentucky State Medical Association, Louisville, Oct. 4-6. Dr. P. E. Blackerby, 620 South Third St., Louisville, Acting Secretary.

Michigan State Medical Society, Detroit, Sept. 22-24. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing, Secretary.

Northern Minnesota Medical Association, Duluth, Aug. 28. Dr. R. N. Jones, 8 Sixth Avenue N., St. Cloud, Secretary.

Oregon State Medical Society, Portland, Sept. 4-5. Dr. Thomas D. Robertson, St. Vincent's Hospital, Portland, Secretary.

Pennsylvania, Medical Society of the State of, Philadelphia, Oct. 5-7. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh, Secretary.

Utah State Medical Association, Salt Lake City, Aug. 27-28. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.

Wisconsin, State Medical Society of, Milwaukee, Sept. 13-15. Mr. Charles H. Crownhart, 110 East Main St., Madison, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

65:681-826 (May) 1943

*Familial Blood Studies in Cases of Mediterranean (Cooley's) Anemia: Diagnosis of Trait, or Mild Form of Disease. C. H. Smith.—p. 681.
*Sulfadiazine: Review of Its Use in Treatment of Children. K. J. Winters and F. R. Janney.—p. 702.
Studies on Vitamin A: Vitamin A and Total Lipid of Serum in Pneumonia. H. W. Josephs.—p. 712.
Treatment of Gonorrheal Vulvovaginitis with Silver Picrate Suppositories: Report of Results in 57 Cases. F. R. Fitch.—p. 728.
Studies in Immunity to Pertussis: II. Effect of Stimulating Dose of Hemophilus Pertussis Vaccine. A. C. Rambar, Katharine M. Howell, E. J. Denenholz, Martha Janota and Roberta Stanard.—p. 730.
Cardiac Muscle in Poliomyelitis. A. R. Peale and P. F. Lucchesi.—p. 733.
Erysipelas in Infancy. J. W. Bruce and T. S. Chalkley.—p. 739.
Nutrition as Conditioning Factor in Rheumatic State. A. F. Coburn and Lucile V. Moore.—p. 744.
Second Attacks of Anterior Poliomyelitis: Report of 4 Cases. N. B. Nelson and W. T. Green.—p. 757.
Pseudoreactions to Tuberculin. H. Vollmer and M. L. Ripps.—p. 763.
Total and Fractional Blood Lipid Levels in Nephrotic Syndrome. Elaine M. Thomas.—p. 770.
Agenesis of Lung in Infant. C. T. Olcott and S. W. Dooley.—p. 776.
*Omphalocele with Congenital Obstruction: Report of Case with Meckel's Diverticulum. H. J. Morrison and R. L. Neville.—p. 781.
Hemangioma of Elbow Successfully Treated with Radium at Early Age. I. I. Kaplan.—p. 785.
Pediatric Aspects of Salem Witchcraft Tragedy: Lesson in Mental Health. E. Caulfield.—p. 788.

Familial Blood Studies in Mediterranean Anemia.—In sixteen families with Mediterranean anemia, 63 persons were examined by Smith and 54 showed abnormalities of the blood. Twelve, all children, were severely anemic and 42, including parents and siblings, had the mild type of this condition. In every one of the sixteen families definite blood changes occurred in at least one parent, and in one family changes were noted in three generations. While all siblings and parents of patients with Mediterranean anemia were examined clinically, hematologically and roentgenographically, the recognition of the mild type depended solely on a careful study of the blood. These changes consisted of varying degrees of hypochromic anemia, occasionally polycythemia, an elevated icteric index, the presence of target cells, reticulocytes, macrocytes and stippled red cells, and increased resistance of the red cells to hemolysis. The most common findings were anisocytosis and poikilocytosis, basophilic stippling and increased resistance to hypotonic sodium chloride solution. Hypochromic and polychromatophilic macrocytes constituted an important diagnostic feature and were frequently found in predominantly microcytic blood smears. Target cells were not a constant accompaniment in all cases, and they appeared in only half of the patients with mild forms of the disease. Thinness and flatness of the cells may represent the fundamental structural defect of the erythrocytes in Mediterranean anemia. Persons with the mild form of the disease were without symptoms and appeared in perfect health, and the condition would have escaped detection without careful scrutiny of the blood. The degree of skeletal change was usually correlated with the severity of the anemia. The later in childhood the disease became manifest, the less severe was the osteoporosis. In every family with a severely anemic child both parents showed abnormalities of the blood, but this cannot be regarded as a universal rule. The children of a parent with the trait run the risk of inheriting the disease in any of its clinical forms from the mildest to the most severe. Since the disease appears to be transmitted directly from parent to child, the implications of the existence of mild forms of Mediterranean anemia are obvious in communities with large Italian and Greek populations. The pedigrees included in this study suggest that Mediterranean anemia is transmitted as a dominant characteristic. Certain features of the blood in Mediterranean anemia resemble those of sickle cell anemia and to a more limited degree those of hemolytic jaundice.

Sulfadiazine in Treatment of Children.—Winters and Janney reviewed hospital records of 90 patients treated with sulfadiazine. The patients varied in age from 3 weeks to 13 years. Conditions treated included infections of the throat, empyema, septicemia, chronic recurrent pyelitis, perirenal abscess, osteomyelitis and meningitis. High blood levels apparently are easily reached and maintained with sulfadiazine because of relatively slow excretion; because of this sulfadiazine may be given at greater intervals or in smaller doses. The drug given to children in doses of ¾ to 1 grain per pound in twenty-four hours will produce an average blood level of 7 to 10 mg. per hundred cubic centimeters, which is adequate for usual infections. Sulfadiazine is effective against most of the common bacteria producing specific infections, especially against hemolytic streptococci, pneumococci, Staphylococcus aureus hemolyticus, meningococci and Hemophilus influenzae. Sulfadiazine passes readily into the spinal fluid. Spinal fluid levels can usually be expected to be two thirds or more of the blood level. With high blood levels or poor intake of fluids, the most common reactions are crystals in the urine, red blood cells in the urine, leukopenia and neutropenia. These signs clear up when the administration of the drug is stopped. Sulfadiazine spray for burns produces a satisfactory eschar and is effective in preventing secondary infection. Patients receiving sulfadiazine should be observed with the same care that is advisable after administration of any other sulfonamide compound, and the urine and the blood count should be checked regularly.

Omphalocele with Congenital Obstruction.—Omphalocele, or exocelom, is a true congenital umbilical hernia containing intestine or abdominal organs. This condition is said to occur once in 5,000 to 6,000 newborn infants. The presence of Meckel's diverticulum in an omphalocele has been reported only twice in the English literature. Neville reports a case in which the intestines could not be reduced until the infant was anesthetized. The size of the omphalocele increased from that of a lemon (approximately 6 cm. in diameter) to that of a medium sized grapefruit (approximately 12 cm. in diameter) within five minutes after birth. This occurred through the swallowing of air when the infant began to cry. The intestines became distended, and this hindered reduction. The infant was operated on when 80 minutes of age. Convalescence was uneventful, and at the age of 14 weeks she weighed 12 pounds 11 ounces (5,755 Gm.) and appeared perfectly normal. Roentgen examination at the age of 5 months failed to reveal the presence of Meckel's diverticulum. This is probably due to the fact that the diverticulum atrophied after the operation.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

49:575-718 (May) 1943

Critical Analysis of Roentgen Signs of Infantile Scurvy. R. S. Bromer.—p. 575.
Calcification of Renal Tumors. G. Austen Jr.—p. 580.
Roentgenologic Examination of Pharynx. S. W. Westing.—p. 587.
Post-Traumatic Necrosis of Bone. R. W. Lewis.—p. 593.
Extraordinary Calcification in Breast. B. W. Anthony and H. C. Pollack.—p. 600.
Osteopoikilosis: Case Report. R. H. Thompson, R. Hoover and H. F. Fulton.—p. 603.
Roentgen Treatment of Cancer of Esophagus. D. W. Smithers, J. R. Clarkson and J. A. Strong.—p. 606.
Roentgen Therapy of "Virus" Pneumonia. A. Oppenheimer.—p. 635.
Radiation Hazards During Roentgenoscopy. T. N. White, D. B. Cowie and A. A. De Lorimier.—p. 639.
Protective Features Provided with United States Army Field Roentgenoscopic Equipment. A. A. De Lorimier, D. B. Cowie and T. N. White.—p. 653.
Studies on Indirect Effect of Roentgen Rays in Single and Parabiotic Mice. W. A. Barnes and O. B. Furth.—p. 662.
Investigation into Some Practical Aspects of Roentgen Ray Stereoptics: Part I. Fallacy in Current Practice of Stereoroentgenography. Part II. Single Film Stereoroentgenography. Part III. Device for Measuring Depth in Single Film Stereoroentgenograms. E. Klein, M. Klein, H. Klein and A. T. Newman.—p. 682.

Archives of Dermatology and Syphilology, Chicago

47:613-762 (May) 1943

Dermatitis Vaccinica (Kaposi's Varicelliform Eruption). F. Ronchese.—p. 613.
Action of Sulfonamide Compounds on Blastomyces Dermatitidis in Vitro. R. O. Noojin and J. L. Callaway.—p. 620.
Superficial Papulonecrotic Tuberculid in Negro. S. Irgang.—p. 627.
Properties of Human Skin Revealed by Fluorescence Microscopy: III. Paraffinoma. T. Cornbleet and H. L. Popper.—p. 637.
*Combined Vaccine and Toxoid Therapy of Staphylococcic Infections of Skin. M. H. Goodman.—p. 640.
Epidermolysis Bullosa. A. G. Franks and M. I. J. Davis.—p. 647.
Vitamin B_6 (Pyridoxine) in Dermatology. C. S. Wright, M. H. Samitz and H. Brown.—p. 651.
Cutaneous Eruptions Due to Codeine. M. Seidmann.—p. 654.
Area Factor in Roentgen Irradiation. G. M. MacKee, A. Mutscheller and A. C. Cipollaro.—p. 657.
Mapharsen and Neoarsphenamine Administered by Continuous Intravenous Drip Method: Toxicity for Rabbits. J. A. Kolmer and Anna M. Rule.—p. 665.
Use of Diethylstilbestrol in Treatment of Kraurosis Vulvae: Preliminary Report. Sadie H. Zaidens.—p. 671.
Bronchial Asthma Following Inhalation of Powdered Neoarsphenamine: Attempted Oral Hyposensitization. J. W. Thomas.—p. 675.
Dermatitis Herpetiformis: Immunologic and Therapeutic Considerations. J. H. Swartz and W. F. Lever.—p. 680.

Staphylococcic Infections of Skin.—According to Goodman, 105 patients with various types of staphylodermas (including 46 with pustular acne) were treated with a combined toxoid-vaccine antigen. Injections were given in increasing doses every fourth day until the tenth dose, of 1 cc. In the usually refractory types of infection, such as pustular acne, treatments were continued in 1 cc. doses with the object of achieving desensitization. By means of this desensitizing regimen it appeared that most of the patients were benefited and a great number obtained what may be justifiably considered a clinical cure. The results of this study are promising and warrant the trial of combined staphylococcus toxoid and vaccine as an adjunct in the treatment of some of the ordinarily stubborn staphylococcic dermatoses.

Archives of Surgery, Chicago

46:589-792 (May) 1943. **Partial Index**

Surgical Approaches to Epiphysial Cartilages of Knee and Ankle Joints. L. C. Abbott and G. G. Gill.—p. 591.
Early Mobilization of Fractures of Upper End of Humerus. F. Brostrom.—p. 614.
Prone Position for Exposing Medial Meniscus of Knee Joint. L. Cozen.—p. 616.
Pseudarthrosis and Neurofibromatosis. W. T. Green and N. Rudo.—p. 639.
Pain in Shoulder Girdle, Arm and Precordium Due to Foraminal Compression of Nerve Roots. S. S. Hanflig.—p. 652.
Arthrogryposis Multiplex Congenita. Miriam Katzeff.—p. 673.
Wire Fixation of Fractures of Proximal Third of Humerus. J. A. Key.—p. 678.
Adventitious Bursas. J. G. Kuhns.—p. 687.
Fracture of Shafts of Both Bones of Lower Half of Leg. J. R. Lincoln and H. Gordimer.—p. 697.
Skeletal Traction as Method of Treatment for Certain Foot Deformities. R. H. Morris.—p. 736.
Subtrochanteric Osteotomy in Coxa Vara. C. W. Peabody.—p. 743.
Internal Brace for Low Part of Back. H. C. Pitkin.—p. 755.
Operation for Correction of Recurrent Dislocation of Jaw. L. D. Smith.—p. 762.
Paratrooper Fracture. W. J. Tobin.—p. 780.
Torsion of Achilles Tendon: Its Surgical Significance. J. W. White.—p. 784.

Arkansas Medical Society Journal, Fort Smith

39:257-270 (May) 1943

Etiology and Treatment of Traumatic or Secondary Shock. C. M. Wilhelmj.—p. 257.

Bulletin of Johns Hopkins Hospital, Baltimore

72:255-308 (May) 1943

Effect of Desoxycorticosterone Acetate Administration on Plasma Volume and Electrolyte Balance of Normal Human Subjects. M. Clinton Jr. and G. W. Thorn.—p. 255.
Behavior of Bipedal Rats. L. W. Pratt.—p. 265.
Studies in Experimental Hypertension: II. Effect of Dietary Protein on Urea Clearance and Arterial Blood Pressure in Chronic Hypertension. L. K. Alpert and Caroline B. Thomas.—p. 274.
Id.: III. Effect of Dietary Protein on Clearances of Diodrast and Insulin by Kidney in Chronic Hypertension. L. K. Alpert and J. L. Lilienthal Jr.—p. 286.
Endocardial Fibroelastosis (So-Called Fetal Endocarditis): Report of 2 Cases Occurring in Siblings. T. Weinberg and A. J. Himelfarb.—p. 299.

Canadian Medical Association Journal, Montreal

48:383-476 (May) 1943

Personnel Selection in Army. W. Line and J. D. M. Griffin.—p. 394.
Psychiatric Problems in Army. D. G. McKerracher.—p. 399.
Canadian Army Medical Corps Training Center. P. N. MacDermot.—p. 404.
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Dermatoscleroses. P. A. O'Leary.—p. 410.
Leiomyosarcoma of Small Intestine. J. A. Rankine.—p. 415.
Dosage of Liver Extract in Treatment of Cord Lesions Associated with Pernicious Anemia. R. Gottlieb.—p. 420.
Some Aspects of Industrial Medicine. R. A. Kennedy.—p. 421.
Accessory Sinus Disease in General Practice. P. G. Goldsmith.—p. 426.
Sinus Problem. K. Hutchison.—p. 431.
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Sensitivity to Pain (with an Analysis of 450 Cases). E. D. Sherman.—p. 437.

Cancer Research, Baltimore

3:281-352 (May) 1943. **Partial Index**

Neoplasm Studies: IX. Effects in Tissue Culture of N,N-Dimethyl-p-Phenylenediamine on Rat Liver Tumors Induced by p-Dimethylaminoazobenzene. Gladys Cameron, M. J. Kopac and R. Chambers.—p. 281.
Effect of Pyridoxine and Other B Vitamins on Production of Liver Cancer with p-Dimethylaminoazobenzene. D. L. Miner, J. A. Miller, C. A. Baumann and H. P. Rusch.—p. 296.
Biocatalysts in Cancer Tissue: II. Inhibition of Succinoxidase System by Tumor Extracts. H. G. Albaum and V. R. Potter.—p. 303.
Experimental Fibroids in Hypophysectomized Female Guinea Pigs. L. Vargas Jr.—p. 309.
Inheritance of Susceptibility to Tumors Induced in Mice: II. Tumors Induced by Methylcholanthrene in Progeny of C3H and JK Mice. W. J. Burdette.—p. 318.
Studies on Spontaneous Tumors in Guinea Pigs: III. Chondrosarcoma of Iliac Bone with Metastasis to Mammary Region. C. T. Olcott and G. N. Papanicolaou.—p. 321.
Intradermal Immunization of C3H Mice Against Sarcoma That Originated in Animal of Same Line. L. Gross.—p. 326.
Distribution of Doses of Radioactive Phosphorus in Leukemic Patients. S. Warren.—p. 334.

Florida Medical Association Journal, Jacksonville

29:455-494 (May) 1943

Changing Trends in Management of Menopause. J. R. Cogan.—p. 465.
Local Use of Sulfonamides in Open Wounds: Review of Present Status. L. J. Netto.—p. 470.
Diagnosis and Treatment of Injury to Spine. H. G. Cole.—p. 473.
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Iowa State Medical Society Journal, Des Moines

33:209-248 (May) 1943

Allergy: Principles of Diagnosis and Treatment. F. K. Hansel.—p. 211.
Analysis of the Rh Factor: H. A. Schwartz.—p. 217.
Diabetes Mellitus Complicated by Urinary Tract Infections. H. Margulies and E. B. Winnett.—p. 219.
Torsion of Appendices Epiploicae: Report of Case. S. D. Porter.—p. 223.
Bronchogenic Carcinoma. F. P. McNamara.—p. 225.

33:249-294 (June) 1943

Medicine in War Effort. C. H. Grahl.—p. 249.
*Massive Arsenotherapy in Early Syphilis by Continuous Intravenous Drip Method: Preliminary Study in Iowa. H. L. Harris and R. M. Sorensen.—p. 254.
Psychopathic Hospital Outpatient Clinic. P. E. Huston.—p. 261.
Multiple Primary Malignant Tumors. F. P. McNamara.—p. 264.

Massive Arsenotherapy in Early Syphilis.—The intensive five day intravenous drip method was used by Harris and Sorensen in 41 cases of early syphilis between July 1940 and July 1942. There were 8 cases of seronegative primary syphilis, 8 of seropositive primary syphilis, 23 of secondary syphilis and 2 of early, latent syphilis. Darkfield examinations were positive in 27. Treatment was started as early as possible. The patients received treatment for five days and were observed for two to three additional days before being discharged from the hospital. Each patient was given 240 mg. of mapharsen in 2,000 cc. of 5 per cent dextrose in isotonic solution of sodium chloride over an eight to twelve hour period daily for five consecutive days. There were no severe reactions such as generalized exfoliative dermatitis or hemorrhagic encephalitis. Twenty-one patients had a primary fever, 10 a secondary fever and 2 a toxicodermic rash. There were no blood dyscrasias, no instances of renal or liver damage and no fatalities. Thirty-six patients experienced arm pain and 24 had nausea and

vomiting at some time during treatment. In order to evaluate this treatment properly the patients must be followed for at least five years. Of the 41 patients reviewed here 32 have been followed from six to eighteen months with 75 per cent satisfactory results, 18.8 per cent pending and 6.3 per cent failures. The patients with seronegative primary syphilis reached a negative status rapidly. Those with seropositive primary syphilis showed more rapid serologic reversals than did those with secondary syphilis. Only 2 of the 41 patients treated had a proved serologic relapse and were retreated by the same method. One of these patients also had an infectious relapse. One patient with probable reinfection was retreated. One patient out of 38 had a positive spinal fluid after completion of treatment. Two weeks later the spinal fluid was normal. Two women were treated during pregnancy without adverse results. This method of treatment has a public health value.

Journal of Allergy, St. Louis

14:273-354 (May) 1943

Studies on Blocking Antibody in Serum of Ragweed Treated Patients: I. Search for Inhibiting Substances in Other Types of Immune Serum. D. E. Frank and H. H. Gelfand.—p. 273.
Comparison of Sodium and Potassium Metabolism of Asthmatic and Nonallergic Children. P. B. Donovan and G. F. Harsh.—p. 281.
Observations on Weltmann Reaction in Hay Fever and Asthma. F. F. Furstenberg and S. Scherlis.—p. 288.
Repeated Bronchial Relaxtion in Treatment of Intractable Asthma. A. L. Barach.—p. 296.
Roentgen Observations on Children with Gastrointestinal Allergy to Foods. J. H. Fries and M. Mogil.—p. 310.
Statistical Studies in Allergy: I. Correlation Analysis. T. G. Andrews.—p. 322.
Sensitivity to Ailanthus Pollen: with Report of 2 Clinically Sensitive Patients. G. I. Blumstein.—p. 329.
Allergy to Food Odors: Its Relation to Management of Infantile Eczema. A. J. Horesh.—p. 335.

Journal-Lancet, Minneapolis

63:87-120 (April) 1943

Tuberculosis—Postwar. K. Emerson.—p. 87.
Importance of Preventive Measures in Tuberculosis Program. S. L. Cox.—p. 88.
Tuberculin Test in Tuberculosis Control. L. L. Collins.—p. 90.
The Doctor of Medicine and His Responsibility. A. W. Adson.—p. 92.
Echinococcus Cyst of Lung. F. E. Torres.—p. 95.
Don't Give Up the Tuberculin Test. O. Lotz.—p. 96.
Tuberculosis Among College Students. H. D. Lees.—p. 98.
Tuberculin Reaction in Medical and Nursing Students: Five Year Study. L. N. Todd.—p. 102.
Examination of Rejectees. H. R. Edwards.—p. 104.
Tuberculosis on Typical College Campus. C. E. Lyght.—p. 108.
Analysis of 149 Tuberculosis Deaths During 1940-41. H. A. Burns.—p. 113.

Medicine, Baltimore

22:87-204 (May) 1943

Immunity in Malaria. L. T. Coggeshall.—p. 87.
*Studies of Calcium and Phosphorus Metabolism with Special Reference to Pathogenesis and Effects of Dihydrotachysterol (A. T. 10) and Iron. S. H. Liu and H. I. Chu.—p. 103.
Anthropometry and Arthritis: I. Differences Between Rheumatoid and Degenerative Joint Disease: Males. C. C. Seltzer.—p. 163.
Id.: II. Differences Between Rheumatoid and Degenerative Joint Disease: Females. C. C. Seltzer.—p. 189.

Calcium and Phosphorus Metabolism and Effects of Dihydrotachysterol in Renal Osteodystrophy.—Liu and Chu report metabolic observations on 5 Chinese patients with various grades of skeletal decalcification with or without other osseous changes occurring in association with moderate to advanced renal insufficiency. The authors apply to this condition the term renal osteodystrophy, pointing out that the term "renal rickets," though used extensively, is objectionable because it identifies the disease of the skeleton with rickets, which it is not in many cases, although the radiologic appearance and the gross deformities of the bones resemble those seen in rickets. The term "renal dwarfism" emphasizes only one feature of the disease which is not present in many cases. Objection to the term "renal infantilism" may be made on the same basis. The term "renal osteodystrophy" seems to be a suitable generic name to include cases of osseous disorder associated with renal insufficiency, while the exact nature of the pathologic process in the skeleton is still undetermined. The bone lesions of the 5 patients varied from slight or moderate osteoporosis with no deformities to pronounced rarefaction with gross deformities. In 2 cases rachitic-like changes were present in the epiphyses. The renal insufficiency was moderate in 1 case and far advanced in the rest. In advanced renal insufficiency difficulty in renal excretion of phosphate was evidenced by a small percentage of urinary phosphorus and by hyperphosphatemia. Such evidence could be brought out more clearly by increasing the phosphorus intake. Calcium balance was negative on low or moderate calcium intake and slightly positive on high calcium intake. High fecal excretion of phosphorus after increased phosphorus intake was usually followed by calcium loss even on high calcium intake. Chronic acidosis was present in all the cases. Alkali administration alleviated the acidosis with improvement of renal function and favorable effect on the calcium metabolism. There was no response to ordinary therapeutic doses of vitamin D and it was meager even to massive doses. In contrast to vitamin D, dihydrotachysterol was remarkably effective in promoting calcium and phosphorus absorption and their deposition in the skeletal store. Iron was efficacious in relieving hyperphosphatemia and in sparing calcium in the intestinal elimination of phosphorus. The lack of response to vitamin D was thought to suggest the possibility of inactivation of vitamin D as a result of functional impairment of the kidney. This was considered to be of primary importance in the genesis of bone disease. A shift of phosphate excretion from the kidneys to the intestine and definite acidosis, present only in advanced renal insufficiency, were important aggravating factors. For treatment a low phosphorus, low protein and high calcium diet, alkali, dihydrotachysterol and iron were indicated. The results with dihydrotachysterol were particularly favorable.

Oklahoma State Medical Assn. Jour., Oklahoma City

36:139-184 (April) 1943

Treatment of War Gases. R. E. Greer.—p. 139.
Hypertension in Young Athlete Due to Coarctation of Aorta: Report of Case. J. A. Blue.—p. 143.
Haverhill Fever: Case Report. W. K. Ishmael.—p. 146.

36:185-230 (May) 1943

*Study of Trachoma with Report of 318 Cases, 233 Treated with Sulfanilamide. C. Gallaher.—p. 185.
Lithokelyphopedion (Lithopedion with Calcified Membranes): Case Report. With Some Remarks on Ectopic Pregnancy in General. G. Penick.—p. 192.
Early Diagnosis of Tuberculosis. T. C. Black.—p. 195.
Intestinal "Decompression": Review of Methods. A. S. Risser.—p. 197.

Trachoma Treated with Sulfanilamide.—Gallaher submits a statistical analysis of 318 cases of trachoma, most of which were treated by him in the course of the last four years. One hundred and eighty-eight of the patients were males and 130 were females; 209 were white, 108 were Indians and 1 was a Negro. Trachoma is rare among the colored population. All except 3 of the patients received ambulatory treatment. The adults numbered 134, the children 184. The author abandoned the use of copper sulfate sticks because of the pain associated with their use. If a treatment is too painful the patients refuse to return. Silver nitrate was used only in case of complication with gonorrheal infections. It was not usually repeated. One or more of the following therapeutic methods were used in all cases: Sulfanilamide by mouth was used in 199 cases, grattage in 26, brossage in 2, zinc sulfate in 58, copper sulfate solution in 46, sulfanilamide (1 per cent in isotonic solution of three chlorides) in 40, sulfathiazole in a 3 per cent ointment in 9 cases, vitamin A (25,000 units or more daily) in 4 cases. The results of sulfanilamide therapy were such that the drug must be included in the treatment of trachoma. No treatment with or without sulfanilamide produces beneficial changes in every case. Well over 90 per cent of cases can be assured of some improvement. Sulfanilamide therapy, in combination with other drugs, affords a method which may be used with reasonable safety without hospitalization and without the necessity of prolonged daily treatment and observation. One or more courses of sulfanilamide alone are apt to produce disappointing results. The specific remedy for trachoma is not yet found. The essential nature of the disease, its cause and its treatment remain a problem to be solved.

Psychosomatic Medicine, Baltimore

5:117-202 (April) 1943

Eating Inhibitions in Children in Relation to Anorexia Nervosa. J. A. Rose.—p. 117.
Studies in Psychosomatics: I. Influence of Hypnotic Stimulation on Gastric Hunger Contractions. J. H. Lewis and T. R. Sarbin. —p. 125.
Relation Between Electromyographic Measurements and Subjective Reports of Muscular Relaxation. J. Ruesch and J. E. Finesinger. —p. 132.
Electroencephalogram in Psychopathic Personality. J. R. Knott and J. S. Gottlieb.—p. 139.
Changes in Electroencephalogram During Cycle of Morphine Addiction. H. L. Andrews.—p. 143.
Further Note on Measurement of Autonomic Balance. M. A. Wenger. —p. 148.
Symposium on Fatigue: H. Davis and others.—p. 152.

Surgery, Gynecology and Obstetrics, Chicago

76:641-758 (June) 1943

*Surgical Management of Some of the More Complicated Problems of Peptic Ulcer. F. H. Lahey and S. F. Marshall.—p. 641.
One Stage Combined Abdominoperineal Resection for Malignant Tumors of Rectum, Rectosigmoid and Lower Part of Sigmoid. C. W. Mayo. —p. 649
Effect of Heparin on Wound Healing. H. Laufman and R. E. Heller. —p. 655.
Use of Venograms for Localization and Study of Arteriovenous Fistula. J. R. Watson, J. M. Lichty, J. M. Hill and R. B. Miller.—p. 659.
Rate of Absorption and Callus Stimulating Properties of Cow Horn, Ivory, Beef Bone and Autogenous Bone. C. W. Hughes.—p. 665.
Congenital Atresia of Esophagus with Tracheoesophageal Fistula: Extrapleural Ligation of Fistula and End to End Anastomosis of Esophageal Segments. C. Haight and H. A. Towsley.—p. 672.
*Traumatic Peritonitis: Choice of Routes for Administration of Sulfonamides. R. K. Gilchrist, F. H. Straus, R. Hanselman, C. C. Draa, S. E. Lawton and M. Freeland.—p. 689.
Distribution of Nerves in Adult Human Myometrium. E. F. Hirsch and Mary E. Martin.—p. 697.
Anterior Sacral Meningocele. F. A. Coller and R. G. Jackson.—p. 703.
Amputations in Children. F. vom Saal.—p. 709.
Primary Carcinoma of Appendix Resembling Carcinoma of Colon. A. Uihlein and J. R. McDonald.—p. 711.
Infiltration Therapy of Acute Tendinitis with Calcification. P. W. Lapidus.—p. 715.
Inhibitory Effect of Procaine on Bacteriostatic Activity of Sulfathiazole. D. Casten, J. J. Fried and F. A. Hallman.—p. 726.
Evaluation of Dysmenorrhea by Basal Body Temperature. R. A. Lyon.—p. 729.
Immediate Active Motion Treatment of Fractures of Head and Neck of Radius. J. A. Mason and N. M. Shutkin.—p. 731.
Rate and Nature of Epithelization in Wounds with Loss of Substance. E. L. Howes.—p. 738.
Construction of an Artificial Vagina. W. M. Adams.—p. 746.

Surgical Management of Peptic Ulcer.—Lahey and Marshall state that, of the 7,000 hospitalized patients with ulcer, 18.1 per cent were subjected to operation for gastric ulcer and 6.59 per cent for a duodenal ulcer. The mortality rate was 2.7 per cent for all gastric, duodenal and gastrojejunal ulcers, exclusive of the gastrojejunocolic fistula; it was 3.2 per cent for 251 subtotal resections of all types—gastric, duodenal, gastrojejunal and gastrojejunocolic fistula; it was 4.4 per cent in 46 consecutive subtotal gastric resections performed solely for a gastrojejunal ulcer. The authors discuss the surgical management of some of the more complicated peptic ulcers in the last 251 consecutive operative cases. The ulcer states which have been complicated and difficult to manage are the low duodenal ulcer involving the common bile duct in its indurated scar, the ulcer located at or below the entrance of the common duct in the duodenum, the gastrojejunal ulcer, the gastrojejunocolic fistula and the recurrent ulcer in the gastric stump after a high subtotal gastrectomy. All the deaths among the 251 patients subjected to total or subtotal gastrectomy for ulcer, with the exception of 1 patient who died of embolus, were of patients having ulcers of these complicated types. The authors stress that conservative operative methods are occasionally imperative to avoid high operative mortality in certain densely adherent duodenal ulcers or ulcers arising low in the duodenum and involving the common duct. Radical subtotal gastrectomy is necessary for relief of the surgical gastrojejunal ulcer. Temporizing operative procedures in view of the possibility of recurrent ulcer serve only to increase further the operative risk.

Sulfanilamides in Traumatic Peritonitis.—Gilchrist and his associates produced peritonitis in dogs to ascertain the time necessary to establish adequate blood and intraperitoneal concentration of various sulfonamides after administration by mouth or vein, by implantation into the abdomen, and by intraperitoneal injection. They made 716 determinations of sulfonamide concentrations on the heart blood and peritoneal fluid in experiments on 75 dogs. The authors present observations on human material which correspond to the results in the animal experiments. Sulfanilamide given by mouth after injury to the peritoneum will not produce adequate early concentrations in blood and peritoneal exudate. A 10 per cent solution of sodium sulfathiazole may be injected intravenously without producing a phlebitis. Fifteen minutes after such an injection the effective sulfathiazole level in the peritoneum will approach that found in the blood. Therapeutic concentration in the peritoneal fluid will be maintained for four to six hours. If sodium sulfathiazole solution is injected into the abdominal cavity after the injury and before closure of the perforation, an immediate high concentration is obtained. When sodium sulfathiazole or sulfanilamide crystals are placed in the abdomen at operation there is a rapid high concentration of drug in the peritoneal exudate. The blood concentration rises to therapeutic levels rapidly and falls below such a level after six hours. When relatively insoluble sulfathiazole crystals are placed in the abdomen, effective concentrations are reached in the peritoneal exudate in twenty minutes and are maintained for many hours. The concentration in the blood rises slowly and usually remains below therapeutic levels. The following program for retarding the development of peritonitis after bowel perforation is suggested: 1. Five-tenths Gm. of sodium sulfathiazole per 10 pounds of body weight should be injected intravenously (5 or 10 per cent solution) in from two to four minutes. Intravenous fluid, plasma, or blood should follow. As an alternate procedure a soluble drug or a suspension of sulfathiazole microcrystals may be injected directly through the abdominal wall or through the entry wound. Laparotomy should be performed as soon as possible. At that time a relatively insoluble sulfonamide, such as sulfathiazole, should be placed in the abdomen. When soluble sulfonamides are used in the abdomen, additional drugs must be administered after eight hours. When slowly soluble sulfathiazole is used in the abdomen, additional drugs need not be administered for twenty-four hours.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

51:177-224 (May) 1943

Problem of Antagonistic (Antigonadotropic?) Substances to Equine Gonadotropin in Clinical Therapy: With Reference to Management of Amenorrhea. J. H. Leathem and A. R. Abarbanel.—p. 177.
Use of Vitamins in Surgery: Résumé. E. F. Gooel.—p. 180.
*Gas Gangrene: Analysis of 416 Collected Cases Treated by Roentgen Therapy with 13 New Cases. K. D. McMilan.—p. 187.
Diseased Tibial Sesamoid of Big Toe Joint. A. Gottlieb.—p. 193.
Fibromyoma of Cervix Uteri Obstructing Labor. R. Torpin.—p. 196.
Influence of Hormones on Varicose Veins in Pregnancy. A. M. McCausland.—p. 199.
Vaginal Antisepsis During Labor: Eleven Thousand Vaginal Deliveries Without Death from Puerperal Infection. H. W. Mayes.—p. 201.

Roentgen Therapy in Gas Gangrene.—McMilan collected from the literature 416 cases of gas gangrene in which roentgen therapy was used and reports 13 new cases in which this treatment was employed. Roentgenograms should be taken of the involved area every four to six hours in injuries where gas gangrene is liable to develop. This will lead to early diagnosis. The development of clinical signs and symptoms need not be awaited. Prophylactic treatment of wounds liable to develop gas gangrene should consist of immediate débridement, use of sulfanilamide in the wound and adequate doses of tetanus gas gangrene antitoxin. X-rays may also be useful as a prophylactic measure. Active treatment should consist of 100 roentgens over involved areas as soon as diagnosis is made or strongly suspected, repeated twice daily for three days or until the infection is brought under control, local débridement and therapeutic amounts of the antiserum if the infection is more than twelve hours old or if the patient does not respond clinically to the foregoing treatment. Amputation should not be resorted to for gas gangrene per se. Of the 416 patients given x-ray treatment 62 died, giving a mortality of 14.9 per cent. Millar's review of 607 cases before the era of roentgen treatment revealed a mortality of 49.7 per cent. Of the 13 newly reported cases 3 had a fatal outcome.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Heart Journal, London

5:73-120 (April) 1943

Chest Lead CR_7 in Cardiac Infarction. W. Evans and A. Hunter.—p. 73.
Potassium Effects on T Wave Inversion in Myocardial Infarction and Preponderance of Ventricle. E. P. Sharpey-Schafer.—p. 80.
Potassium Effects on Electrocardiogram of Thyroid Deficiency. E. P. Sharpey-Schafer.—p. 85.
Anginal Pain in Myxedema. A. A. F. Peel.—p. 89.
Common Aortopulmonary Trunk: Rare Congenital Defect. C. W. C. Bain and J. Parkinson.—p. 97.
Fatal Coronary Thrombosis in Man Aged 22. W. S. Miller and W. W. Woods.—p. 101.
Syphilitic Angina Pectoris. E. Jones and D. E. Bedford.—p. 107.

British Medical Journal, London

1:623-654 (May 22) 1943

Investigations During an Outbreak of Bullous Impetigo Neonatorum. T. H. C. Benians, with technical assistance of J. Webster and A. G. Newman.—p. 623.
Blood Transfusion in Nocturnal Hemoglobinuria. J. V. Dacie and D. Firth.—p. 626.
Treatment of Psychiatric Patients in General Hospitals: Social Experiment. D. E. Sands.—p. 628.
Atropine Glaucoma. J. E. Martin.—p. 631.
Specifications for Dark Adaptation Tests. K. J. W. Craik.—p. 632.
Critic of Bishop Harman Test for Night Vision. J. Yudkin, in collaboration with A. Ferguson.—p. 633.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

50:83-160 (April) 1943

Present Position of Antenatal Care in Obstetrics. J. D. Green.—p. 83.
Investigation of Effect of Ergot Alkaloids in Promoting Involution of Postpartum Uterus. C. Moir and C. S. Russell.—p. 94.
*Further Bacteriologic Studies of Severe Clostridium Welchi Infections Following Abortion. Hildred M. Butler.—p. 105.
Anesthesia and Analgesia in Obstetrics from Viewpoint of General Practitioner. J. Elam.—p. 120.
Tuberculosis of Female Genital Tract. O. Browne.—p. 128.
Clinical Significance of Degree of Calcification of Placenta as Demonstrated by X-Ray Photography. Amy M. Fleming.—p. 135.
Traction on Groin in Breech Presentation. M. Wassermann.—p. 140.
Hemangioma of Arm Causing Delay in Delivery and Neonatal Death. Mildred I. Ealing.—p. 144.
Uterus Didelphys. Nora L. Keevil.—p. 146.

Clostridium Welchi Infection Following Abortion.—At the Woman's hospital in Melbourne as many as twelve deaths in one year have resulted from fulminating infections due to Clostridium welchi. It is often present in the vagina, the uterine contents, the urine and even in the blood without causing symptoms of a severe infection. Thus mere isolation of Cl. welchi from the tissues or body fluids is of little diagnostic significance. Butler showed that the strains of Cl. welchi causing the severe infections differed from most of the strains obtained from patients who did not develop symptoms both in regard to growth characteristics and to the amount of capsular material produced in broth. The examination of smears from the cervical canal solved the problem of rapid bacteriologic diagnosis. In severe infection cervical smears showed heavily capsulated bacilli and considerable destruction of the leukocytes. This combination was not seen in the smears from patients who, although infected with Cl. welchi, did not show symptoms of a severe infection. This suggested that severe Cl. welchi infections associated with abortion were caused by only certain variants of this organism. She studied more than 600 strains of Cl. welchi isolated from abortional cases with regard to one or more of the following characteristics: capsulation in broth cultures, production of alpha toxin, phagocytosis by human leukocytes and pathogenicity of washed cultures for guinea pigs. Smears from the cervical canal were examined in 80 cases in which there was a proved Cl. welchi infection. All the strains of Cl. welchi causing the severe generalized infection possessed the properties of highly invasive variants and differed from both the strains causing localized infections and those cultivated from the blood of patients without symptoms of a severe Cl. welchi infection. In the severe infections the patient's symptoms were correlated with the properties of the infecting strain. The comparative rarity of the severe infections was explained by the finding that the highly invasive variants of Cl. welchi formed only a small minority of the strains cultivated from the genital tract. All the strains causing the severe infections and also some of the control strains produced a fatal infection in guinea pigs when washed cultures from agar were injected intramuscularly. This property was sometimes lost comparatively rapidly under artificial cultivation. It is suggested that a somewhat similar correlation to that observed in abortional cases may exist between severity of infection and the characteristics of the infecting strain in gas gangrene following wounding.

Lancet, London

1:637-668 (May 22) 1943

Blood Volume in Chronic Anemia by Concentrated Corpuscle Hemoglobin Method. J. McMichael and E. P. Sharpey-Schafer.—p. 637.
Vitamin C. Subnutrition in Gingivostomatitis. F. Stuhl.—p. 640.
Necrotic Gingivitis. B. S. Kent.—p. 642.
*Iron Media for Cultivation of Anaerobic Bacteria in Air. Nancy J. Hayward and A. A. Miles.—p. 645.
Sulfapyridine Anuria. A. L. Kerr.—p. 646.
Anuria from Tubular and Ureteric Obstruction Following Sulfapyridine Therapy. W. Thompson.—p. 647.
Sulfapyridine Anuria and Its Treatment. W. A. Flynn.—p. 648.
Pneumococcic Meningitis: Recovery with Sulfamethazine. R. Pakenham-Walsh.—p. 649.

Iron Mediums for Cultivation of Anaerobic Bacteria in Air.—Hayward and Miles found that strips of sheet iron (which is a heat resistant, moderately pliable type of rolled mild steel) have a remarkably stimulating effect on the growth promoting properties of simple solutions of peptone for anaerobic bacteria. The mode of action of the iron is probably complex. The maintenance of a stock of dry strips of sheet iron is a simple matter, and broths or peptone waters from which air has been expelled by heating are converted by the strips into excellent "aerobic" mediums for biochemical tests of anaerobic bacilli, both sporing and nonsporing, and of anaerobic streptococci.

Medical Journal of Australia, Sydney

1:341-358 (April 17) 1943

*Bacillary Dysentery Caused by Bacterium Dysenteriae P274. L. E. Rothstadt, F. Fenner and B. A. Baker.—p. 341.
*Bacillary Dysentery: Some Results and Conclusions from Series of Patients Treated with Sulfaguanidine. R. F. West.—p. 344.

Bacillary Dysentery Caused by Bacterium Dysenteriae P274.—Rothstad and his collaborators provide further evidence for the acceptance of P274 as a true dysentery organism. They review cases of dysentery treated at an Australian general hospital. Stools from 228 patients suspected of having bacillary dysentery were examined, and dysentery organisms were isolated from 85, as follows: Bacterium dysenteriae Flexner, 39; Bacterium dysenteriae P274, 42; Bacterium dysenteriae Boyd I, 1; Bacterium dysenteriae Sonne, 2; Bacterium dysenteriae Schmitz, 1. Bacterium dysenteriae P274 was not isolated from any patient not suffering from clinical dysentery and has not been reported to occur in normal stools in numerous examinations. The clinical picture of the disease caused by P274 is indistinguishable from that of acute bacillary dysentery due to Bacterium dysenteriae Flexner. The authors conclude that the organism P274 of previously unproved pathogenicity has satisfied the criteria necessary to secure its acceptance as a true dysentery bacillus. It is suggested that the organism should be named "Bacterium dysenteriae Boyd IV."

Bacillary Dysentery Treated with Sulfaguanidine.—West made a survey of 279 patients with diarrhea admitted to a hospital over a period of three months. Early diagnosis is important, and in most cases it can be made from the history and from macroscopic examination of the stools. Laboratory methods are a help but are not necessary for diagnosis. Sigmoidoscopic examination is essential in all doubtful cases. Among the 279 cases there were 167 of acute bacillary dysentery, 12 of amebic dysentery and 100 of nonspecific enteritis. Limitation of bed space permitted complete treatment of only 97 of the patients with bacillary dysentery. Attempts at culture with 1 specimen of feces from each of the 97 patients yielded results in 46 (48 per cent). The types of organisms isolated were Flexner I, Flexner II, Shiga, Schmitz and Sonne. A control series of 23 patients were treated with sodium sulfate, the other 74 being treated with sulfaguanidine. Patients treated

with sulfaguanidine showed a pronounced improvement in their general condition after twenty-four hours, and on the third day their feeling of well-being was remarkable; this is in sharp contrast to those receiving saline therapy, who even at the end of seven days, and sometimes well into the second week, experienced abdominal discomfort, anorexia and malaise. The authors conclude that sulfaguanidine therapy should be used in all cases, mild or severe.

Schweizerische medizinische Wochenschrift, Basel

72:1289-1312 (Nov. 21) 1942. **Partial Index**

Estimation of Operability of Patients with Diabetes Mellitus: Their Preoperative and Postoperative Treatment. G. R. Constam.—p. 1289.
Practical Suggestions for Treatment of Caries. F. Oesch.—p. 1292.
Calcium Metabolism. G. Schönholzer.—p. 1295.
Osteoid of Cortical Part of Bone: Differential Diagnosis of Bone Changes. A. Fehr.—p. 1298.
*Studies on Problem of Goiter: Goitrogenic Substances in Plants and Sensitivity of Animals. F. Blum.—p. 1301.
*Ergotamine Tartrate in Herpes Zoster. A. Stökly.—p. 1305.
Spontaneous Cure of Gastric Perforation. M. Roch.—p. 1307.

72:1313-1340 (Nov. 28) 1942. **Partial Index**

Thrombosis and Pulmonary Embolism in Relation to Meteorologic Changes at Altitude of Davos (1,550 Meters Above Sea Level). W. Stähli.—p. 1321.
Cases of Epidemic Cerebrospinal Meningitis with Encephalitic Complication. E. Kovács and I. Faragó.—p. 1326.
Influence of Vitamin B1 on Carbohydrate Metabolism. O. Osman Saka.—p. 1327.
*Studies on Problem of Goiter: Goitrogenic Substances in Plants and Sensitivity of Animals. F. Blum.—p. 1329.
Treatment of Insomnia. F. Grote.—p. 1333.

Goitrogenic Substances in Plants.—Blum states that practically all members of the cabbage (Brassica) family except kale contain goitrogenic substances. Soy beans have a strumigenic effect as do also various beans which are members of the Phaseolus family, and peas and lentils, members of the Vicia family. There are indications that peanuts (Arachis) contain a strumigenic factor. He found that not only small animals like rats, guinea pigs and rabbits are likely to develop goiter in response to feeding with the aforementioned vegetables but also goats, sheep and hogs. Typical goitrous degeneration of the thyroid could be developed in dogs provided the feeding with cabbage was begun early enough and was sufficiently prolonged. Geese likewise developed characteristic thyroid changes.

Ergotamine Tartrate for Herpes Zoster.—Friis-Møller found ergotamine tartrate highly effective in herpes zoster. Stökly administered 0.5 cc. of ergotamine tartrate subcutaneously for six successive days in the treatment of 6 patients with herpes zoster. The results obtained corroborated those of the Danish author. With the exception of nausea and vomiting in 2 cases there were no untoward effects. Five of the 6 patients showed considerable improvement after the second injection. The peripheral circulation must be carefully controlled in the course of the treatment. Ergotamine tartrate is contraindicated in severe cardiac insufficiency and in Raynaud's disease. Stökly modified the dosage in 6 new cases by giving 0.5 cc. on the first day and 1 cc. daily after that until an effect could be noticed and then resumed the 0.5 cc. dose. The total dose varied between 4.5 and 6 cc. The treatment was successful in all 12 cases.

Prensa Médica Argentina, Buenos Aires

30:549-596 (March 31) 1943. **Partial Index**

Bronchopulmonary Cancer Without Clinical Symptoms or X-Ray Signs. M. R. Castex and E. S. Mazzei.—p. 553.
*Cervical Rib in Pulmonary Tuberculosis. H. Butori.—p. 558.

Cervical Ribs and Pulmonary Tuberculosis.—Butori observed 3 cases of cervical rib simulating pulmonary apical tuberculosis. He reviewed roentgenograms of 3,500 patients with pulmonary tuberculosis and found either a cervical rib or hypertrophy of the transverse process of the seventh cervical vertebra in the roentgenograms of 32 out of 1,100 women and of 12 out of 2,400 men, an incidence of 2.9 and 0.5 per cent for women and men respectively. The ribs were bilateral in 27 and unilateral in 12. The right bilateral rib was longer than the left in the majority of the cases. A right unilateral rib was more frequent than the left (7 to 5). The first rib of either side showed abnormalities in 9 cases. These consisted of asymmetrical atrophy of the arch and of the presence of insertions of supernumerary muscles between the first rib and the cervical rib. Heredity and syphilis were not involved as causal factors. The Kahn serum test was negative in all but 2. There was no relationship between the type of pulmonary tuberculosis and the presence of a cervical rib. The existence of a cervical rib does not predispose to pulmonary tuberculosis. A cervical rib may simulate tuberculosis because of an area of dulness to percussion over the supraclavicular fossa, because of diminished respiratory excursions and because of certain subjective symptoms such as pain and nervous symptoms common to the two conditions.

Revista Clínica Española, Madrid

7:301-362 (Dec. 15) 1942. **Partial Index**

Wounds of Large Intestine Caused by Firearms: Observations on 212 Cases. A. G. Barón.—p. 301.
Studies on Fat Metabolism: Existence of Fat Mobilizing Substance in Animals with Ligated Choledochus. C. Jiménez Díaz and H. Castro Mendoza.—p. 318.
*Existence of Substances Inhibiting Reaction of Carr-Price in Some Vitamin Products. M. A. Catalán and F. Grande Covián.—p. 321.
Macrogenitosomia (Pubertas Precox) of Cerebral Origin: "Diencephalic" or "Hypothalamic" Forms (Berblinger). M. Schachter.—p. 324.
*Vitamin E and Neuromuscular Syndromes. P. Puig Muset.—p. 328.
Application of Beer's Law on Color Development in Carr-Price Reaction of Vitamin A. M. A. Catalán and F. Grande Covián.—p. 340.
Aplastic Anemia Caused by Benzene: Myeloblastic Leukemia. G. Paniagua.—p. 341.

Substances Inhibiting Carr-Price Reaction in Vitamin A Products.—Catalán and Grande Covián state that cod liver oil and vitamin A preparations contain substances which inhibit the color reaction of the antimony trichloride color test of Carr-Price. They tried to obtain quantitative information regarding the inhibiting factors. They determined the inhibiting effect exerted by various quantities of chloroform dilutions of cod liver oil. The presence of substances inhibiting the Carr-Price reaction are of importance in the chemical evaluation of vitamin A; because of them the vitamin A content of some preparations may be underestimated and of others overestimated. If the vitamin A content of an oil is to be determined, it should be ascertained first whether it contains inhibiting factors detectable by saponification. A systematic study should be made of the distribution of inhibiting substances in various natural oils, which would establish the method to be employed in the evaluation of each particular oil. Commercial products of vitamin A often consist of vitamin A concentrates diluted in various types of oils. These oils may contain substances that inhibit the color reaction. Thus a change in the diluting oil may result in a noticeable change in Carr-Price color reaction although the vitamin A content is the same.

Vitamin E for Neuromuscular Syndromes.—Puig Muset reviews observations reported by histopathologists on neuromuscular lesions resulting from diets deficient in vitamin E, as well as experimental investigations carried out by himself. He believes that vitamin E acts on the muscular system by fixing the phosphatides which form myelin. He deduces from this that, in order to be effective, vitamin E requires the presence of phosphatide reserves in the organism or the external administration of these substances. He regards lathyrism as a disease which exemplifies a deficiency in phospholipoids.

Revista Paulista de Medicina, São Paulo

21:153-250 (Sept.) 1942. **Partial Index**

*Meta-Amino-Parahydroxyphenyl Arsine Hydrochloride Hemialcoholate in Therapy of Syphilis. J. de Alcantara Madeira.—p. 153.
Female Hormones in Therapy of Hemophilia. T. Niemeyer.—p. 237.

Meta-Amino-Parahydroxyphenylarsine Hydrochloride Hemialcoholate in Syphilis.—Alcantara Madeira administered this substance to 150 adult patients with primary, secondary and tertiary syphilis. The drug was given intravenously in 0.04 Gm. doses. The injections were given once a week for twelve injections. Two courses of injections were given one month apart. The treatment produced a rapid healing of primary, secondary and tertiary lesions and a rapid conversion of serologic tests. The drug was well tolerated.

Book Notices

New and Nonofficial Remedies, 1943, Containing Descriptions of the Articles Which Stand Accepted by the Council on Pharmacy and Chemistry of the American Medical Association on January 1, 1943. Issued Under the Direction and Supervision of the Council on Pharmacy and Chemistry of the American Medical Association. Cloth. Price, $1.50. Pp. 772. Chicago: American Medical Association, 1943.

New and Nonofficial Remedies for 1943 continues, with minor improvements, the convenient and informative system of classification adopted for the 1942 volume. The terminology of the official drugs has been revised to conform to the U. S. P. XII and the N. F. VII. The valuable bibliographic index now appears on white instead of "India tint" paper, a wartime necessity. This index appears before the general index, which is now more properly placed at the end of the book. The new arrangement may appear at first somewhat awkward, but with a little use the wisdom and convenience of the changes become more and more apparent.

The chapter on digitalis and digitalis-like principles and preparations has been extensively and somewhat radically revised to keep pace with the changing attitude toward this drug. In this revision the Council had the aid of the foremost authorities on digitalis, including pharmacologists and clinicians. It is interesting to contrast the following sentence in the 1942 general article on Chaulmoogra Derivatives: "The therapeutic properties of chaulmoogra oil appear to be due to these optically active unsaturated fatty acids of the chaulmoogric series," which in the 1943 edition reads "Any therapeutic properties chaulmoogra oil may possess would appear to be due to these optically active unsaturated fatty acids of the chaulmoogric series."

Among the more noteworthy of the new editions are nikethamide, the central nervous system stimulant which was first introduced as coramine; diethylstilbestrol, the synthetic estrogen; trichinella extract for the diagnosis of trichinosis, and zephiran chloride, a mixture of alkyl dimethyl benzyl ammonium chlorides, an interesting new anti-infective agent.

The successive volumes of New and Nonofficial Remedies increase the profound respect everywhere tendered to the faithful and unselfish work of the Council on Pharmacy and Chemistry in the cause of rational therapeutics. Each volume represents a progressive milestone on the road of medical science.

Final Report, White House Conference on Children in a Democracy, Washington, D. C., January 18-20, 1940. United States Department of Labor, Children's Bureau Publication No. 272. Paper. Price, 65 cents. Pp. 392, with illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1942.

This is the final report of the conference which met in Washington, Jan. 18-20, 1940. Since its adjournment follow-up committees have been organized in twenty-six states and in Puerto Rico. The report outlines the point of view and perspectives of the conference and presents studies relating to child health and welfare in the American democracy. First there is a report on the numbers and distribution of children, followed by a discussion of the American setting, rural and urban, economic and cultural. The situation faced by children of minority groups is discussed, with special reference to inequalities and discriminations. A chapter is devoted to the common needs of all children—parents, family life, dwelling, health, protection, education and training, and preparation for later life. A chapter devoted to economic problems results in the interesting conclusion, among others, that "one of the principal objectives of sound economic life in a democracy is that people shall be able to earn and administer their own incomes," but over against this on the same page, and part of the same set of conclusions, appears "In pursuance of this function it would seem unavoidable for the government to assume a far larger and more responsible share in the direction of the national economy than has been the case in the past. The provision of services to the people so as to achieve a more equitable distribution of the wealth produced is only one way—although a very important one—of achieving that end." Education, leisure time activities and employment receive attention in lengthy chapters, and so do social services for children.

The considerable space devoted to health will be of special interest to the doctor. The general tenor of the attitude of the conference seems fairly represented by the following:

> It is coming to be recognized that a very large part of the population, in addition to "the indigent," cannot, from their own resources, meet the expense of proper medical care and that in the long run it will pay "the public" to supply hospital accommodations, laboratory facilities and other diagnostic aids, use of therapeutic appliances, medical and nursing service, and convalescent care for all the "medically needy."

On this point the recommendations of this conference include the following specific statement:

> The health and well-being of children depend to a large extent upon the health of all the members of their families. Preventive and curative health service and medical care should be made available to the entire population, rural and urban, in all parts of the country. A considerable portion of the population is able to obtain from its own resources all or part of the necessary medical service. Another large section of the population, however, consists of families whose incomes are below the level at which they can reasonably be expected to budget all the varying costs of illness without interfering with the provision of other items essential to the family's health and welfare; for these there should be available adequately supervised medical and dental care through a program financed by general tax funds, social insurance systems, or such combination of methods as may be best suited to local conditions.
>
> To achieve these ends will require expansion of full time local public health services organized on a city, county or district basis; construction and adequate support of health centers and hospitals as needed, especially in rural areas, and more effective use of existing medical services and facilities; more effective coordination of community public health and medical services conducted by various agencies, public and private.
>
> "More money will have to be spent by government at all levels—local, state and federal. The responsibilties of each—administrative as well as financial—will have to be defined. The confusing array of agencies, public and voluntary, will have to be brought into a comprehensible system."

Nutrition: An Introductory Text. By Fern Silver, Supervisor of Home Economics, Lincoln High School, Albuquerque. Cloth. Price, $1.35. Pp. 168, with illustrations. New York: D. Appleton-Century Company, 1942.

This is a brief outline of nutrition intended for home use. It has chapters on foods in relation to energy and growth—composition, fuel value, fuel requirements, protein and its uses, and digestion and absorption—minerals in relation to body nutrition, vitamins, planning an adequate diet, adequate diets for children, and relation of adequate diet to health. There is a general knowledge test on nutrition, an appendix containing tables of food values, and an index. In general the material is useful and well selected. The section on vitamins could have been improved by reducing emphasis on the results of extreme vitamin deficiencies amounting to virtual absence. Xerophthalmia and beriberi are not seen often in this country; the speculation as to whether sciatic rheumatism may be due to vitamin B_1 deficiency is out of place in such a book. More emphasis on subclinical deficiencies and less on extreme deprivation would be more serviceable in a book intended for lay readers. The table of food values on pages 140-143 is exceptionally good, bringing together all the contributions of ordinary servings of common foodstuffs. The tables of food composition beginning on page 151 are less serviceable—calories per pound are seldom of interest; protein, carbohydrate and fat in percentages require too much mathematics for the average—or even the above average—home. The material in this book is excellent for nutritionists and advanced students; its presentation is not as practical as it could have been for the ordinary American home.

Synopsis of Pathology. By W. A. D. Anderson, M.A., M.D., Assistant Professor of Pathology, St. Louis University School of Medicine, St. Louis. Cloth. Price, $6. Pp. 661, with 311 illustrations. St. Louis: C. V. Mosby Company, 1942.

From the author's preface "This volume is intended to fill a gap which has existed between the very elementary manuals of pathology and the abundant excellent larger textbooks and reference works. By the presentation of pathology in a compact and condensed form, it is designed to be useful to the medical student, to the dental student studying general pathology, and to the clinicians who must maintain familiarity with the foundation sciences of medical practice." In the first edition of a textbook such as this, one expects to find a certain number of errors and instances of disproportion. This book is singularly free from such defects. It is remarkably well balanced and admirably reflects the author's purpose. Approximately 23 per cent of the text is devoted to general pathology (of which 60 per cent deals with infectious disease), 5 per cent to oncology and 72 per cent to special pathology. Illustrations

are quite adequate and, for the most part, excellent. Seventeen tables are to be found throughout the text, e. g. on differential features of venereal lesions, vitamin deficiencies in man, inflammations and ulcerations of the intestinal tract and grading of carcinoma of the cervix, which present in schematic fashion and correlate various related pathologic entities. It is fortunate that, in spite of space limitations, the author has seen fit to include in the chapters devoted to special pathology a brief concise summary of pertinent anatomic and physiologic data and thus prepare for a more complete understanding of the abnormal. The selection of references which may be found at the end of each chapter is especially to be commended in that the majority of them date from 1940. In the opinion of the reviewer this textbook is excellent in all respects and accomplishes what the author intended.

Holt's Care and Feeding of Children. Revised and Enlarged by L. Emmett Holt Jr., M.D., Associate Professor of Pediatrics, Johns Hopkins University, Baltimore. [Sixteenth edition.] Cloth. Price, $2. Pp. 321, with 5 illustrations. New York & London: D. Appleton-Century Company, Inc., 1943.

This book has been standard ever since the first edition appeared half a century ago. Since that time many things have happened, and the Holts, father and son, and their manual have had a part in them. Infant lives have been saved, health and feeding problems have been conquered, until the problem is not so much keeping children alive as teaching them to live and learning to live with them. The latest edition of Holt's manual takes cognizance of behavior problems, and deals with them in the same simple practical way as with directions about how to wash diapers and how to feed the baby artificial formulas as ordered by the doctor. The manual is a question and answer book, and it covers literally everything that a young mother would want or need to know. This edition can be recommended as whole heartedly as previous ones have been.

Human Neuroanatomy. By Oliver S. Strong and Adolph Elwyn, Associate Professor of Neuroanatomy, College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, $6. Pp. 417, with 320 illustrations. Baltimore: William Wood & Company, 1943.

This excellent book is a real contribution for the undergraduate as well as the graduate student. It is written on the premise that neurology is dependent on an accurate knowledge of anatomy as a basis for the intelligent diagnosis and localization of neural disturbances. With this premise the reviewer entirely agrees. There are twenty chapters. The first eight describe in detail the organization of the central nervous system with regard to embryology, histology, segmental distribution of the peripheral nerve elements and their significance. The next twelve chapters are devoted to the study of the architectonics of the central nervous system. Here one finds excellent gross and microscopic photographs of anatomic detail with a clearcut discussion of the relationship of the structures in the light of clinical experience. There are three hundred and twenty such photographs. There is a large bibliography. This is a good book and is highly recommended.

Vitamins and Hormones: Advances in Research and Applications. Edited by Robert S. Harris, Associate Professor of Nutritional Biochemistry, Massachusetts Institute of Technology, Cambridge, Mass., and Kenneth V. Thimann, Associate Professor of Plant Physiology, Harvard University, Cambridge. Volume I. With a foreword by E. V. McCollum. Cloth. Price, $6.50. Pp. 452, with illustrations. New York: Academic Press, Inc., 1943.

The contents of this book are not as general and all inclusive as the title may suggest; they are devoted to special considerations which give the volume added value. The chapter titles include choline—chemistry and significance as a dietary factor; the appraisal of nutritional states; physical methods for the identification and assay of vitamins and hormones; the chemical and physiologic relationship between vitamins and amino acids; the photoreceptor function of the carotenoids and vitamin A; the significance of the vitamin content of tissues; growth factors for protozoa; physiology of anti-pernicious anemia material; the intermediate metabolism of the sex hormones; the hormones of the adrenal cortex. All sections are prepared by investigators prominent in the respective fields. Some of the information is presented in unique fashion, some as a redigestion of previously known or suspected facts; all offers a worthwhile reference source for those interested in vitamins and hormones. Sometimes a suspicion of the contributor's inclination in controversial subjects is apparent, but this does not detract from the usefulness of the book; for the critical reader it should do no more than stimulate further thought.

Doctors of the Mind: The Story of Psychiatry. By Marie Beynon Ray. Cloth. Price, $3. Pp. 335, with illustrations by Ruth Ray. Boston: Little, Brown and Company, 1942.

The book gives popular and vivid but withal reliable accounts of some phases of scientific and practical psychiatry in recent times. Certain noteworthy achievements in psychiatry are described, largely on the basis of personal observations and interviews with leaders in the field, coupled with results of research of past records of the literature. No effort is made to review systematically the basic history of psychiatry and neurology. That mental illnesses long regarded as incurable are now in some cases curable is emphasized hopefully and effectively.

Atlas of Obstetric Technic. By Paul Titus, M.D., Obstetrician and Gynecologist to the St. Margaret Memorial Hospital, Pittsburgh. Cloth. Price, $7. Pp. 180, with 193 illustrations by E. M. Shackelford, Medical Illustrator, John C. Oliver Memorial Research Foundation, St. Margaret Memorial Hospital. St. Louis: C. V. Mosby Company, 1943.

Titus presents the subject of obstetric technic in pictorial form. In addition there are sections on sterility and minor postpartum complications treated in the same manner. The illustrations were prepared from sketches made in the delivery and operating rooms; hence they are accurate. The author claims that the book has a function entirely its own, namely the teaching of both normal and operative obstetrics by visual means through the medium of carefully prepared illustrations. However, there are few illustrations which cannot be found in the standard textbooks on obstetrics. Nevertheless some of the intermediary steps shown in this book are not in the standard textbooks and they may prove helpful to many physicians and medical students. A few additional illustrations should have been included. These are illustrations showing the knee-chest and Trendelenburg positions for the immediate treatment of prolapse of the cord, local anesthesia for vaginal deliveries and cesarean section, and the use of a tracheal catheter or some other apparatus for the resuscitation of the newborn. The illustrations are magnificent and unsurpassable for purposes of instruction. Each step is clearly shown, and the person looking at them should have a perfect visual image of every operative obstetric procedure. Titus deserves great credit for preparing such a fine atlas because, when used in conjunction with one of the standard textbooks of obstetrics, it should prove to be most valuable.

Children Can Help Themselves: The Normal Child's Health Behavior. By Marion Olive Lerrigo, Ph.D. Cloth. Price, $2.25. Pp. 219. New York: Macmillian Company, 1943.

This book was written for parents. In a narrative form the author introduces a sensible pair of young parents and shows by concrete examples how they reared their son. In respective chapters the reader sees David at 1, 4, 8, 12 and 18 months, then at 2, 3, 4, 5, 8 and 11 years. The customary health behavior of the child at these stages of development is portrayed in each chapter. In each are included the diet, sleep, training, exercise and mental development at these various stages. As David gets older his behavior is checked against that of his two favorite playmates. The aim of the book is to aid parents as they impart responsibility and self reliance to the offspring. The fascinating style of each chapter should hold the young parents' attention through the years.

Peresadka rogovitsy svezhim konservirovannym i fiksirovannym materialom; eksperimentalnie i klinicheskie nablyudeniya. [By] O. I. Shershevskaya. [Corneal Transplantation of Fresh, Preserved and Fixed Tissues: Experimental and Clinical Observations.] Boards. Pp. 201, with 80 illustrations. Novosibirsk, 1940.

The monograph by O. T. Shershevskaya, submitted for the degree of master of science, deals with the subject of transplantation of the sclera. The author has reviewed the literature on the subject very well. She reports her own experiments with transplantation of the sclera in rabbits, utilizing fresh and conserved as well as tissue fixed in solution of formaldehyde. Much credit is given to the pioneer work in this field by Filatov.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SUDDEN DEATH AND ANESTHESIA—FUNDAMENTALS OF ANESTHESIA

To the Editor:—**A white woman aged 21, whose weight was 110 pounds (50 Kg.), requested a tonsillectomy. Her past history was negative except that she had always been nervous. Preoperatively her heart, lungs, blood pressure and urinalysis were normal. The patient was given morphine sulfate ⅛ grain (0.008 Gm.) and atropine sulfate 1/200 grain (0.00032 Gm.) one-half hour before operation. Induction of anesthesia was begun with approximately 50 drops of chloroform and was continued with ether. No further chloroform was used. The operation was slightly prolonged. The anesthesia was rather light, the pupils being moderately constricted and there being some motion of the eyeballs most of the time. In fact, I found it difficult to maintain sufficient depth with ether vapor administered through an ether tube attached to a suction machine and had to supplement this, because of movement of the patient's limbs, with drop ether on three different occasions. Ether was omitted entirely during the last fifteen minutes because of faulty respirations and pallor. The pupils did not dilate. During the last fifteen minutes of the operation the patient stopped breathing momentarily and respirations were easily started by the simple procedure of pressure on the sternum. Immediately on removal of the mouth gag and completion of the operation, the respirations were Cheyne-Stokes in type. They persisted thus until death by respiratory failure one and one-quarter hours after completion of the operation. The pupils were dilated between 2.5 and 3 mm. They dilated widely with the apneic phase and contracted with the hyperpneic phase. The heart action was good until the last. Nikethamide, caffeine and epinephrine were given with temporary benefit but without interrupting the periodic character of the respirations. Is it likely that I am right in assuming that death was due to morphine idiosyncrasy? Could death, under similar circumstances, be caused by acapnia resulting from partial and intermittent anesthesia and holding the breath during induction? Could the chloroform have influenced the result? In this case would atropine, in the dose given, decrease or augment the respiratory depression? Can any reliance be placed on pupil signs with the use of morphine and atropine or either drug alone? Should morphine be condemned as preoperative medication? I do not consider this an ether death because the respirations did not stop but became periodic, the patient lived one and one-quarter hours after stoppage of ether, and the narcosis, instead of becoming lighter with elimination of the ether, became deeper and more profound. Does the literature record many deaths during ether induction from acapnia? Can ether narcosis produce Cheyne-Stokes respirations? Have any similar accidents been recorded? Is it likely that the use of carbon dioxide-oxygen mixture (not available at the time) would have made any difference in the outcome? Is lobeline a more powerful respiratory stimulant than nikethamide? Sollmann states in his textbook of pharmacology that it is dangerous to give an anesthetic to a crying child because of the possibility of producing acapnia. Has clinical experience borne this out? Is it advisable to give preoperative medication before tonsillectomy to infants and small children? Which is the safest sedative for preoperative use, morphine or one of the barbiturates? Is carbon dioxide administration effective in overcoming acapnia?**

M.D., New York.

ANSWER.—Explanation of the sudden death of a healthy person is not always possible. The excitement attendant on such an occurrence often prevents accurate recording of events and their sequence. The fact that thorough postmortem examination has failed on many occasions to furnish proof of the cause of death is well recognized. Before attempting to answer the fourteen questions included in this communication, it may be profitable to offer some general comment on anesthetic problems.

Incidental interference with the normal physiologic functions accompanying the state of anesthesia are the usual causes of morbidity and mortality rather than specific effects of particular drugs. In other words, failure adequately to protect the functions of respiration and circulation during anesthetic depression is of vastly greater importance than is the choice of the drugs used or the doses administered. In this case no mention is made as to whether the anesthetist was able to maintain completely free and unobstructed breathing throughout the operation. Not infrequently, respiratory obstruction is present during a tonsillectomy under general anesthesia unless an artificial airway is placed in the trachea. Even with minimal bleeding during such an operation, blood and mucus may pass through the trachea into the lungs and interfere seriously with the exchange of oxygen and carbon dioxide between alveoli and the blood. On the basis of the information given, the most likely explanation of this accident would seem to be respiratory obstruction. In some patients the anatomic relation of the structures of the pharynx when the mouth is held wide open results in partial obstruction of the larynx. Inadequate depression of the reflexes in the throat may result in partial adduction of the vocal cords, thus contributing a considerable degree of obstruction to breathing. Clotted blood or pharyngeal secretion in the air passages in the lungs may prevent either partly or completely the exchange of atmosphere in a lobule, a lobe or even a whole lung beyond the obstruction. Any of these accidents may be superimposed on what would otherwise be an insignificant depression of respiratory exchange due to the central action of sedative drugs or of general anesthetic agents. Granted that such partial respiratory obstruction did persist during this operation, the cells of the centers governing respiration would suffer from lack of oxygen and from acidosis caused by accumulated carbon dioxide. The physiologic mechanism for the maintenance of normal breathing is dependent on these two factors, the tension of oxygen and of carbon dioxide. The possibility of such disturbances resulting in serious harm or even in death is appreciated by the experienced anesthetist.

In answering the specific questions as accurately as may be, page references are made to the book Fundamentals of Anesthesia published by the American Medical Association Press, 1942.

1. The effective dose of morphine varies with individuals. Rarely is an eighth of a grain found to cause alarming symptoms even in a 5 year old child (p. 32 and following of Fundamentals).

2. Acapnia or depletion of carbon dioxide can cause death only through the failure of breathing. Artificial respiration is the remedy. The opposite condition, sometimes called hypercapnia, is much more likely during general anesthesia (p. 21 and following).

3. Death during the administration of chloroform is possible but not under the circumstances described.

4. Atropine in usual doses is not a likely cause of respiratory depression. It increases the rate of breathing and decreases the depth. It tends slightly to decrease the respiratory depression from morphine for this reason (top p. 37).

5. Whether morphine is used to advantage before inhalation anesthesia depends on the time interval, on the dosage and on recognition by the anesthetist of its pharmacologic effects (p. 32). It may accomplish tranquillity and allay fear. It carries the patient toward anesthesia, and the quantity of other drugs needed (ether, for example) is reduced. The time of its maximum depressant effect on respiration is roughly ninety minutes after hypodermic administration. Hence it is rarely given within one hour of induction of inhalation anesthesia, so that depression of ether may not be superimposed on an unexpected depression from the opiate. However, respiratory depression from the morphine may decrease respiratory exchange sufficiently to make saturation of the patient with ether difficult (pp. 133, 134 and 135 of Fundamentals).

6. Death from acapnia is likely only if respiration ceases in the presence of hypoxia and artificial respiration is not instituted.

7. Cheyne-Stokes respiration during ether anesthesia is usually due to hypoxia following respiratory depression or obstruction, usually the latter (p. 19).

8. Similar accidents have been observed and recorded. They have often been considered the result of long continued obstruction to respiration and an inadequate supply of oxygen. The sudden relief of obstruction without adequate excess oxygen in the atmosphere and in the presence of drug depression of the respiratory centers results in a complicated physiologic condition which may be fatal.

9. The use of an atmosphere rich in oxygen might have been very useful in this case. It seems justifiable to believe that the use of oxygen, of artificial respiration during the apneic periods, and the establishment of free exchange by means of an artificial airway might have changed the outcome. Whether carbon dioxide would be of added value is a debatable point.

10. It is probable that neither lobeline, nikethamide nor any other stimulant would have had a beneficial result. Many anesthetists prefer artificial respiration to stimulating drugs because it is efficient and instantly available (chapter VIII, p. 151).

11. During crying, deep breaths alternate with breath holding. Irregularity of dosage results. Anesthetic drugs are administered to crying children without accidents. It is perhaps cruel but not "dangerous" if proper safeguards are taken. To avoid the necessity of doing so, many anesthetists administer to children sedative drugs preoperatively in rather large doses.

12. Some anesthetists consider it advisable to administer nonvolatile drugs to children before tonsillectomy. Others do not. Factors other than age and weight must influence the dosage of depressant drugs administered to children (pp. 51 and 52).

13. It cannot be said that morphine is "safer" than one of the derivatives of barbituric acid. One ought to be familiar with the pharmacologic effects of the drugs which one uses and choose drugs and doses which will produce effects desirable in the patient to whom they are administered (pp. 32 and 38).

14. Since acapnia results from excessive elimination of carbon dioxide (hyperpnea), administration of this gas should overcome the acapnia. However, rarely during inhalation anesthesia does excessive elimination of carbon dioxide occur. On the other hand, an accumulation of carbon dioxide in the blood and body tissues during anesthesia is almost impossible to prevent because depression and obstruction of respiration are so frequently present (p. 23).

PROGNOSIS AFTER CORONARY OCCLUSION AND DEVITALIZED TEETH

To the Editor:—A man aged 40 had a nearly fatal anterior coronary occlusion in December. Since that time he has been making as much recovery as we think could be expected and with the exception of occasional pain and some limitation is going about his business. Some years ago three Caldwell-Luc operations were performed on his right antrum. Since that time he has had a sensory disturbance of his right upper lip and the right lower part of his nose. The internist who took care of the patient during his cardiac difficulty advised that all foci be checked and removed. Two upper teeth on the right side of his head, bicuspid and first molar, have never given any known trouble and are perfectly sound to inspection and to x-ray examination but will not give any response to vitality tests. The question which the dentist, internist and I do not feel competent to answer is Should these two teeth be extracted or should they be left in? The patient, while perfectly willing to cooperate, is not anxious to have the teeth extracted unless there is very good reason for it, since their loss would require replacement by dentures in order to leave enough teeth for chewing. How good would you judge this patient's prognosis for life? The electrocardiogram following the attack showed definite changes in the chest leads. The limb leads showed no changes for several weeks and then showed a decreased amplitude of the R wave in the first lead and coving and inversion of the T waves in all leads. Since that time the limb leads have appeared normal except for some decreased amplitude. There never was any appreciable disturbance in the take-off of the ST segment in the limb leads. There was considerable such disturbance in the chest leads.

M.D., Kansas.

ANSWER.—Despite the fact that some residual angina pectoris is suggested by the statement in the second sentence of the query and the necessarily guarded prognosis in any case of coronary heart disease, it is possible that this man may feel perfectly well after a few more months and live for a good many years if his heart is not appreciably enlarged and if he has the usual luck and takes reasonable care of himself. His age is in his favor. The electrocardiogram, although of some importance, should not be the preponderant factor in prognosis. It is not apparent that there exists the necessity to have the teeth removed for the sake either of his heart or of his face, simply because they are devitalized, though the heart would probably stand the operative procedure.

FAMILIAL ONYCHOLYSIS

To the Editor:—A 6 months old child had two toenails on each foot grow away from the nail floor instead of adhering to it. The mother has had a similar condition all her life and it has proved a nuisance. Is there any way of so directing the growth of the nail by strapping or any other method that will eventually make it grow normally?

E. T. Wilkes, M.D., Sunnyside, L. I., N. Y.

ANSWER.—Onycholysis, separation of the nail plate from its bed for a part of its extent, is one of the commoner diseases of the nails. It is most often secondary to skin disease, such as psoriasis, eczema, syphilis or verruca, involving the nail folds or nail bed, or to trauma and maceration as in the series of occupational cases reported by Templeton (H. J.: Onycholysis, an Industrial Dermatosis, THE JOURNAL, Dec. 26, 1931, p. 1950). There are reports, however, of onycholysis of familial origin. These cases are frequently ascribed to familial endocrine disturbance, for onycholysis has been seen in hyperthyroidism and hypothyroidism, hypogonadism and hypopituitarism. Thyroid disturbances seem to cause it much oftener than the other endocrine dysfunctions, and E. C. Fox has given an excellent report of a series of such cases (Diseases of the Nails: Report of Cases of Onycholysis, *Arch. Dermat. & Syph.* **41**:98 [Jan.] 1940). Of his 30 cases, 28 occurred in women, most of them with low basal metabolism. Of these 3 were secondary to psoriasis or lichen planus, and 3 others could not be observed long enough to judge the effect of the treatment. Of those who were treated adequately with thyroid, 3 failed to improve, 21 showed definite improvement and several of these relapsed when the treatment was stopped. Definite signs of deficiency of the thyroid may be wanting, yet the patient improves when given thyroid therapy.

Concerning the possibility of mechanical aid to correct this condition, the only reference which has been found was the recommendation of J. Heller (Onycholysis, *Handb. d. Haut- u. Geschlechtskr.*, Berlin, Julius Springer, 1927, p. 113) to bind the nails with strong preparations of tar, ichthammol or salicylic acid. No report of the success or failure of such measures has been discovered.

OIL SOLUBLE SUBSTANCES FOR INTRAMUSCULAR INJECTION

To the Editor:—Will you please tell me what is known regarding the absorbability of medical agents dissolved in oil and injected hypodermically or intramuscularly? For instance, can any dependence be placed in the acutely stimulating effect of camphor dissolved in oil and injected? Mexican doctors in general use this agent by this method in cases in which an acute stimulant is required, and I contend that it is an erroneous procedure.

J. A. King, M.D., Santiago Papasquiaro, Mexico.

ANSWER.—There are in general three classes of oil soluble substances which are used for intramuscular injection. The first is soluble in oil but is insoluble in water and in tissue fluids. The second is soluble in oil and in tissue fluids but is insoluble in water. The third class is oil soluble volatile substances.

In the first case the substance is precipitated in the tissues and absorption is poor. It generally causes a local fibrosis, and painful nodules may result.

In the second class, as illustrated by mercuric salicylate and bismuth subsalicylate, the substance is soluble in the tissue fluids. They are carried through the lymph spaces and reach the interstices in the muscles, where they form droplets and may become almost encysted. The oil is later digested and the substance is gradually absorbed over a period of weeks. This gives a reservoir of the drug for continued absorption. Such drugs are usually given once a week.

In the third class volatile substances such as camphor may be absorbed independent of the oil. However, ampules of camphor have recently been omitted from N. N. R. (THE JOURNAL, Feb. 6, 1943, p. 431).

POSITIVE SEROLOGIC TEST FOR SYPHILIS WITHOUT PHYSICAL SIGNS

To the Editor:—A man aged 30 on routine preemployment examination was found to have a 4 plus Kahn and Wassermann reaction at a reliable laboratory. Careful physical examination, including x-ray of chest and careful questioning, reveal no evidence of syphilis. Repeated blood serologic tests after several days remain positive. Assuming that this could be a false positive reaction, what is the maximum length of time I am ethically justified in waiting to start active treatment? It has been my observation and the opinion of several of my colleagues that many if not the majority of physicians in this locality would start active treatment immediately. Would I be legally liable if this person should develop a tertiary lesion in the interval of waiting to see if this reaction becomes negative?

M.D., Missouri.

ANSWER.—A suggested method of study of the problem of biologic false positive serologic tests is contained in an article by Joseph Earle Moore, Harry Eagle and Charles F. Mohr (Biologic False Positive Serologic Tests for Syphilis: III. A Suggested Method of Approach to Their Clinical Study, THE JOURNAL, Nov. 9, 1940, p. 1602).

Among the points suggested in that paper is the performance of serial quantitatively titered blood serologic tests over a period of time in order to determine whether the reagin titer is falling, as would be expected in most biologic false positive tests; or alternatively remaining stationary or rising, as would be expected in syphilis. Assuming that this type of observation is carried out, together with the other points mentioned in the article referred to, it is justifiable to wait for six months to start active treatment.

So far as is known, the question of legal liability in the event of development of a syphilitic lesion during the interval of waiting has never been determined. No opinion could be expressed of the action of a hypothetical court if and when such a case ever came to trial.

OPTIC ATROPHY NOT DERIVED FROM ATABRINE

To the Editor:—Have you any information on the possibility of atabrine causing progressive optic atrophy? We have at present a soldier with optic atrophy which we believe may be due to this drug, which he was taking while on Guadalcanal. All other tests have been negative. I shall appreciate any information which you may be able to give me pertaining to this subject.

Captain, M. C., A. U. S.

ANSWER.—There are no recorded instances of any individual developing progressive optic atrophy following the use of atabrine. Complete observations are available on large immediate dosages as well as prolonged administration of the drug. It is probable that such a condition develops independently and is not associated with the drug.